```
Set     Items   Description
S1    1945000   S FETUS?? OR FOETUS?? OR FAETUS?? OR FETAL? OR FOETAL? OR FAETAL? OR
EMBRYO? ? OR EMBRYONIC? OR UNBORN? OR (UN OR "NOT" OR PRIOR OR BEFORE)(2W)(BORN??? OR
BIRTH???) OR (PRE()TERM? ? OR PRETERM?)(5N) (BABY? ? OR BABIES OR CHILD? ? OR CHILDREN? OR
OFFSPRING? OR OFF()SPRING? ?)
S2     296311   S IN()(UTERO OR VIVO OR VENTER) OR PRE()NATAL??? OR PRENATAL? OR (INSIDE
OR IN OR WITHIN)(3N)(UTERUS? OR WOMB? ? OR UTERI? ?)
S3     179144   S VIABLE? OR VIABILIT? OR ALIVE OR LIVE OR LIVES OR LIVED OR LIVING OR
SURVIV?
S4       6553   S (MAINTAIN? OR SUSTAIN? OR CONTINU?)(3N)(PREGNANCY OR PREGNANT) OR
(CARRY? OR CARRIE? ?)(2N)(TERM? ? OR FULLTERM?)
S5     353928   S HARVEST? OR BIOPSY? OR BIOPSIE? ? OR SAMPLING? OR SAMPLE? ? OR REMOV? OR
EXTRACT? OR RESECT? OR WITHDRAW? OR COLLECT? OR EXCIS??? OR EXCISION? OR OBTAIN??? OR
(TAKE? ? OR TAKING OR TOOK)()OUT
S6      83327   S S1 (5N) S5
S7      96258   S S5 (5N) (TISSUE? ? OR BONE OR MASS OR SPECIMEN? OR SAMPLE? ?)
S8      56858   S S1(5N)S3
S9       7576   S S2(5N)S5
S10       261   S S6:S7 AND S8 AND S9
S11        30   S S10/2002:2004
S12        46   S S10/2005:2008
S13       185   S S10 NOT S11:S12
S14        91   RD  (unique items)
S15     30033   S S5(5N)S1(5N)(TISSUE? ? OR BONE OR MASS OR SPECIMEN? OR SAMPLE? ?)
S16       262   S S2 AND S15 AND S8
S17        39   S S16/2002:2004
S18        46   S S16/2005:2008
S19       220   S S16 NOT (S13 NOT S17:S18)
S20       110   RD  (unique items)
S21        79   S S2 AND S15 AND S4
S22         5   S S21/2002:2004
S23         8   S S21/2005:2008
S24        66   S S21 NOT (S13 OR S22:S23)
S25        36   RD  (unique items)
S26        73   S S6:S7 AND S4 AND S9
S27         2   S S26/2002:2004
S28         2   S S26/2005:2008
S29        69   S S26 NOT (S13 OR S27:S28)
S30        40   RD  (unique items)
S31       176   S (S20 OR S25 OR S30)
S32       173   RD  (unique items)

?  show files
```

[File 155] **MEDLINE(R)** 1950-2008/May 14
(c) format only 2008 Dialog. All rights reserved.
**File 155: MEDLINE has reloaded. Please see HELP NEWS 155 for details.*

[File 73] **EMBASE** 1974-2008/May 15
(c) 2008 Elsevier B.V. All rights reserved.
**File 73: The 2008 EMTREE Thesaurus has been loaded. Please see HELP NEWS 72 for details.*

[File 5] **Biosis Previews(R)** 1926-2008/May W2
(c) 2008 The Thomson Corporation. All rights reserved.

[File 91] **MANTIS(TM)** 1880-2008/Aug
2001 (c) Action Potential. All rights reserved.

[File 164] **Allied & Complementary Medicine** 1984-2008/May

?

Contract/Grant No.: AI-27741; AI; United States NIAID; HE-53754; United States PHS
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
To investigate the mechanism of HIV-1-induced hematopoietic abnormalities, we examined the effect of HIV-1 infection on the in vitro and **in** vivo behavior of precursor cells **obtained** from human **fetal bone** marrow (HFBM). After infection with the monocyte-tropic isolate HIV-1(ADA), HFBM cells displayed a significant decrease in their subsequent in vitro production of precursor cell colonies and a marked impairment in their engraftment of the bone marrow of irradiated SCID mice. By injecting retrovirally tagged, purified human CD34+ cells into HIV-1(ADA)-infected or uninfected human thymic tissue implanted in SCID mice, we demonstrated that HIV-1 infection also inhibited the in vivo differentiation of CD34+ cells into T cells. To determine the mechanism by which HIV-1 suppressed hematopoietic activity, we investigated whether HIV-1 infection induced apoptotic cell death in hematopoietic cells. Multiparameter flow cytometry with FITC-labeled annexin V and propidium iodide demonstrated that infection of the HFBM with monocyte-tropic, but not T cell line-tropic HIV-1, stimulated apoptosis in the CD34+ hematopoietic precursor population. The presence of a TNF-alpha inhibitor during exposure of the HFBM cells to HIV-1 substantially reduced the level of apoptosis of CD34+ cells and significantly decreased the repression of in vitro colony formation induced by HIV-1. However, inhibition of TNF-alpha during HFBM cell culture with HIV-1 did not restore their capacity to engraft SCID mice. Taken together, these results indicated that HIV-1 suppression of human hematopoietic cell maturation is a multifactoral phenomenon, a crucial element of which may be HIV-1-induced apoptosis of precursor cells mediated by TNF-alpha production.
Record Date Created: 20000120
Record Date Completed: 20000120

14/7/15 (Item 15 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

12856492 **PMID:** 9790364
Fetal lung lesions: management and outcome.

Adzick N S; Harrison M R; Crombleholme T M; Flake A W; Howell L J
The Center for Fetal Diagnosis and Treatment at the Children's Hospital of Philadelphia, Pennsylvania 19104, USA.
American journal of obstetrics and gynecology (UNITED STATES) Oct 1998 , 179 (4) p884-9 , **ISSN:** 0002-9378--Print **Journal Code:** 0370476
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
OBJECTIVE: Our purpose was to review our experience with fetal congenital cystic adenomatoid malformation and extralobar pulmonary sequestration emphasizing natural history, management, and outcome. STUDY DESIGN: We conducted a retrospective review of 175 fetal lung lesions diagnosed by antenatal ultrasonography at 2 fetal treatment centers. RESULTS: There were 134 congenital cystic adenomatoid malformation cases. Fourteen women underwent elective abortion, 101 women were managed expectantly, 13 women had fetal surgery, and 6 women had

placement of a thoracoamniotic shunt. For the congenital cystic adenomatoid malformation lesions that were not associated with nonimmune hydrops, all babies survived. Of 25 large congenital cystic adenomatoid malformations that had associated hydrops that were followed expectantly, all fetuses died before or shortly after birth. **Fetal** surgical **resection** of the tumor (**fetal** lobectomy) was performed at 21 to 29 weeks' gestation in 13 hydropic fetuses with 8 fetuses continuing gestation with subsequent hydrops resolution, impressive in utero lung growth, and neonatal **survival**. Six **fetuses** with a very large solitary cyst underwent thoracoamniotic shunting and 5 survived. There were 41 extralobar pulmonary sequestration cases. Twenty-eight extralobar pulmonary sequestrations dramatically regressed on serial prenatal sonography, were asymptomatic after birth, and were only detectable by imaging studies postnatally (no resection required). Of the remaining 13 extralobar pulmonary sequestration cases, 2 underwent elective abortion, 7 symptomatic lesions were resected after birth with **survival**, 1 hydropic **fetus** died, and 3 fetuses had an associated tension hydrothorax with secondary hydrops that was successfully treated by either fetal thoracenteses or thoracoamniotic shunting followed by postnatal **resection**. CONCLUSIONS: The natural history of **prenatally** diagnosed lung masses is variable, and associated anomalies are rare. Most congenital cystic adenomatoid malformation lesions can be managed with maternal transport, planned term delivery, and postnatal resection. Many extralobar pulmonary sequestrations dramatically decrease in size before birth and may not need treatment after birth. Fetal therapy is now an option for lung lesions associated with nonimmune hydrops.
Record Date Created: 19981110
Record Date Completed: 19981110

14/7/20 (Item 20 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options

12414241 **PMID:** 9354883
In utero partial liver resection in the rabbit model: a study on fetal tissue regeneration.

Patricolo M; Zangari A; Paolocci N; Magni F; Viola-Magni M P; Hernandez-Mena L A; Capuano L; Rivosecchi M
Department of Pediatric Surgery, Bambino Gesu Children's Hospital, Rome, Italy.
Fetal diagnosis and therapy (SWITZERLAND) Jul-Aug 1997 , 12 (4) p232-5 , **ISSN:** 1015-3837--Print
Journal Code: 9107463
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
In this study we developed a model of **in** vivo intrauterine partial liver **resection** in the **fetal** rabbit to analyze fetal liver regeneration. After intravenous anesthesia, 12 time-dated pregnant, California rabbits underwent a midline laparotomy and minimal hysterotomy at 24-25 days of gestational age. One fetus was exposed from each pregnant doe and the **fetal** liver was partially **resected**. Cesarean sections were performed 24, 48 and 72 h and 4 days after surgery. Three fetuses operated at 24 days of gestational age and 3 **fetuses** operated at 25 days were alive at retrieval. The **fetuses** and the **sampled** livers were weighed at retrieval and fetal liver weight showed a well-maintained value in all cases. Fetal livers were processed for the common histologic stains. Lymphocytes, polymorphonuclear leukocytes and phagocytes were counted from sections obtained in areas close to the edge of resection. Inflammatory cells showed a peculiar pattern of infiltration at different stages of repair, with a constantly increased number of phagocytes peaking 48 h after **resection**. **Fetal** liver seems to present a specific pattern of repair that differs from both the adult liver and other fetal tissues healing after injury.

Record Date Created: 19971204
Record Date Completed: 19971204

14/7/37 (Item 37 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09347264 **PMID:** 2324262
Assessment of the viability and pregnancy potential of mouse embryos biopsied at different preimplantation stages of development.

Krzyminska U B; Lutjen J; O'Neill C
Human Reproduction Unit, Royal North Shore Hospital of Sydney, St Leonards, NSW, Australia.
Human reproduction (Oxford, England) (ENGLAND) Feb 1990 , 5 (2) p203-8 , **ISSN:** 0268-1161--Print
Journal Code: 8701199
Publishing Model Print
Document type: Comparative Study; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The developmental potential in vitro and **in** vivo of preimplantation mouse **embryos biopsied** at the 4-cell, 8-cell and morula stages were investigated. Biopsy had the least impact when performed at the 8-cell stage. There was no effect of biopsy on the development of 8-cells of blastocysts in vitro (95% compared with 99% of controls) or the implantation rate after transfers (82 versus 87%, P greater than 0.05); however, fewer embryos (52 versus 71%, P less than 0.05) resulted in **viable fetuses**. There was no effect of **biopsy** at the 8-cell stage on fetal weight on day 17. Blastocyst formation in vitro was significantly less for 4-cell biopsies compared with their controls (76 versus 90%, P less than 0.001) and biopsy also affected the implantation rate (44 versus 59%, P less than 0.01). Biopsy was most detrimental when performed on morulae, reducing the implantation rate from 65% for controls to 21% for **biopsies** (P less than 0.001). **Fetal viability** was also markedly affected with a reduction on day 17 from 42 to 26% accompanied by a significant reduction (24%, P = 0.02) of the mean **fetal** weight. Handling of **embryos** for **biopsy** at the morula stage, which involved removal of the zona pellucida, was a significant but not complete cause of the reduced implantation potential observed (sham-controls and intact-controls: 34 and 65%, P less than 0.001), while puncture of the zona during the biopsy of 4-cell and 8-cell embryos had no effect. Therefore, the 8-cell mouse embryo is the most suitable state for **embryo biopsy**.
Record Date Created: 19900515
Record Date Completed: 19900515

14/7/45 (Item 45 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

05740634 **PMID:** 102031
Neuronal plasticity in primate telencephalon: anomalous projections induced by prenatal removal of frontal cortex.

Goldman P S
Science (New York, N.Y.) (UNITED STATES) Nov 17 1978 , 202 (4369) p768-70 , **ISSN:** 0036-8075--Print
Journal Code: 0404511
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
When the dorsolateral prefrontal cortex in one hemisphere of a rhesus monkey is **resected** 6 weeks **before birth** and the **fetus survives** to postnatal ages, neurons of the corresponding cortex in the intact hemisphere issue a greatly expanded projection to the contralateral caudate nucleus in addition to a normal projection to the ipsilateral caudate. The enhancement of the crossed prefronto-caudate pathway after prenatal neurosurgery provides direct evidence for lesion-induced neuronal rearrangement in the primate telencephalon.
Record Date Created: 19790124
Record Date Completed: 19790124

14/7/51 (Item 3 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0075739276 **EMBASE No:** 1994149700
Embryo survival after pronuclear microinjection and trophectoderm biopsy

Burwinkel T.H.; Kim H.-N.; Buster J.E.; Minhas B.S.; Carson S.A.
Div. of Reproductive Endocrinology, Department of Obstetrics/Gynecology, University of Tennessee, 956 Court Ave., Memphis, TN 38163, United States
Corresp. Author: Carson S.A.
Corresp. Author Affil: Div. of Reproductive Endocrinology, Department of Obstetrics/Gynecology, University of Tennessee, 956 Court Ave., Memphis, TN 38163, United States

American Journal of Obstetrics and Gynecology (AM. J. OBSTET. GYNECOL.) (United States) June 10, 1994 , 170/4 (1199-1203)
CODEN: AJOGA **ISSN:** 00029378
Document Type: Journal ; Article **Record Type:** Abstract
Language: English **Summary language:** English

Objective: Our purpose was to compare murine embryo development after pronuclear microinjection of a gene construct, followed by trophectoderm biopsy at the blastocyst state, with development after a single micromanipulation, and with cultured controls. Study design: alpha-Myosin heavy-chain gene sequence was microinjected into the murine embryo pronucleus and cultured to blastocyst. After trophectoderm **biopsy** the **embryos** were allowed to reexpand. Reexpanded embryos were transferred to pseudopregnant females; implantation and live birth rates were recorded. In this study group the rates were compared with three control groups of embryos simultaneously cultured after (1) pronuclear microinjection only, (2) trophectoderm biopsy only, and (3) nonmicromanipulated, culture only. Results: A total of 1222 embryos were divided among the four groups. In the study group 472 **embryos** underwent pronuclear microinjection and trophectoderm **biopsy**. Of these, 203 (43%) reached the blastocyst stage and underwent biopsy; 183 (38.8%) reexpanded after biopsy. Of 275 pronuclear

EMBASE

0073143036 **EMBASE No:** 1986177070
Chorionic villus sampling in continuing pregnancies. I. Low fetal loss rates in initial 109 cases

Elias S.; Simpson J.L.; Martin A.O.; et-al
Section of Human Genetics, Prentice Women's Hospital and Maternity Center, Chicago, IL 60611, United States
Corresp. Author Affil: Section of Human Genetics, Prentice Women's Hospital and Maternity Center, Chicago, IL 60611, United States

American Journal of Obstetrics and Gynecology (AM. J. OBSTET. GYNECOL.) (United States) September 4, 1986 , 154/6 (1349-1352)
CODEN: AJOGA **ISSN:** 00029378
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

Among the first 150 women who agreed to have chorionic villus sampling after receiving counseling and giving informed consent, 41 proved ineligible. In six (5.5%) of the remaining 109 cases in which chorionic villus sampling was performed, we were unsuccessful in obtaining an adequate amount of villi to permit diagnostic testing. In the single loss, **fetal viability** was confirmed 2 weeks after **sampling**; however, **fetal** death became evident 3 weeks later. In four (3.7%) cases the pregnancies were terminated because of abnormal results, and in one (0.9%) case the pregnancy was electively terminated after normal results. Among the 41 completed pregnancies no anomalies were evident in the infants. There were two premature deliveries; one of these two infants died shortly after birth following premature rupture of the membranes at 29 weeks' gestation. All undelivered cases were progressing normally at the time of submission.

14/7/57 (Item 9 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0073133018 **EMBASE No:** 1986167052
Cytogenetic analysis of chorionic villi: A technical assessment

Vekemans M.J.J.; Perry T.B.
Department of Pediatric Pathology, The Montreal Children's Hospital, Montreal, Que. H3H 1P3, Canada
Corresp. Author Affil: Department of Pediatric Pathology, The Montreal Children's Hospital, Montreal, Que. H3H 1P3, Canada

Human Genetics (HUM. GENET.) (Germany) August 27, 1986 , 72/4 (307-310)
CODEN: HUGED **ISSN:** 03406717
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

Eighty-five **samples** of chorionic villi from women undergoing prenatal diagnosis at 8 to 12 weeks' gestation were subjected to cytogenetic analysis. **Samples** were prepared by a direct technique that permits limited analysis within

two hours and by a short-term culture technique that permits detailed structural analysis within one week. An adequate number of cell divisions for cytogenetic analysis was **obtained** from 96% of **living fetuses**. Using both the direct technique and short-term culture, satisfactory banded chromosomal preparations were made in 93% of cases. Eleven of 12 pregnancies (92%) shown by ultrasound to be dead shortly before sampling, had cytogenetic abnormalities. Further studies are needed to develop banding definition equivalent to that available on cultured amniocytes.

14/7/58 (Item 10 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0072693496 **EMBASE No:** 1984123912
Possible source of error in prenatal diagnosis via chorionic villus biopsy

Ridler M.A.C.; Grewal M.S.
Kennedy-Galton Centre, Harperbury Hospital, Radlett, Herts WD7 9HQ, United Kingdom
Corresp. Author Affil: Kennedy-Galton Centre, Harperbury Hospital, Radlett, Herts WD7 9HQ, United Kingdom

Lancet (LANCET) (United Kingdom) July 12, 1984 , 1/8385 (1081)
CODEN: LANCA **ISSN:** 01406736
Document Type: Journal ; Letter **Record Type:** Abstract
Language: English

Chorionic villus biopsy has been hailed as a desirable alternative to amniocentesis as a source of fetal cells for prenatal diagnosis. The technique is less invasive and permits earlier screening (and thus earlier termination of pregnancy if indicated). Chorionic villus biopsy has not yet fulfilled its early promise, however, mainly because of variable success in obtaining villi good enough for culture or direct preparations for karyotyping. Additionally, the risk to the fetus, compared with that of amniocentesis, has yet to be determined - and with chorionic biopsy the likelihood of contamination with maternal cells is greater. Two recent reports are relevant to the risks and errors attendant upon chorionic biopsy. One author reports that the risk of spontaneous abortion is increased earlier in gestation and with higher maternal age but falls to a level common to all maternal ages at about 14 weeks' gestation. For a maternal age of 40 or over, the risk is very small at the usual gestational age for amniocentesis but is increased by a factor of 5 or more at the earlier stage at which chorionic biopsy is done. Two other investigators draw attention to a possible source of error which may arise when trophoblast **biopsy** is used in **prenatal** diagnosis. Artifactual mosaicism was more common in trophoblastic than in fetal tissue. The proposed explanation for this observation was that a very early single nondisjunction could produce mosaicism retricted to either fetus or placenta and that, in the blastocyst, the disproportionately greater number of cells forming the placenta will result in an increased frequency of placental mosaicism. Maternal contamination and in-vitro artifact have always been problems with amniotic cell culture. Analysis of replicate clones or cultures will exclude most errors, but the difficulty of predicting fetal phenotype in the presence of prenatal mosaicism remains a cause for anxiety. The use of trophoblast material must increase the risk of error, which must be seen as significant until shown to be otherwise. The example of mosaicism for chromosome 20 illustrates the dilemma. This is one of the most common mosaics found in amniotic fluid cultures which may be genuine or artifact. The mosaicism may or may not be detectable in the fetus but there has so far been no conclusive demonstration of phenotypic abnormality in a **fetus** or **live**-born infant. The origin of trisomy-20 amniotic cells has not been defined and it has been suggested that trophoblast is implicated,

though this explanation may be questioned when fetal mosaicism is found. In one case study, trisomic cells were present in the fetus but their detection in only one of two **biopsy specimens** from placental membrane supports the present argument. Furthermore there is a natural tendency to attach greater significance to abnormal cells found in an otherwise normal preparation, but possible error may equally occur from the presence of non-representative normal cells produced by non-disjunction in a trisomic conceptus. For both of these reasons, it would seem prudent to proceed with caution in substituting chorionic villus biopsy for amniocentesis as a routine method of prenatal screening for chromosomal abnormality.

14/7/76 (Item 15 from file: 5) **Links**
Fulltext available through: STIC Full Text Retrieval Options
Biosis Previews(R)

05666594 **Biosis No.:** 197967055589
NEURONAL PLASTICITY IN PRIMATE TELENCEPHALON ANOMALOUS PROJECTIONS INDUCED BY PRE NATAL REMOVAL OF FRONTAL CORTEX

Author: GOLDMAN P S (Reprint)
Author Address: LAB NEUROPSYCHOL, NATL INST MENT HEALTH, BETHESDA, MD 20014, USA**USA
Journal: Science (Washington D C) 202 (4369): p 768-770 1978
ISSN: 0036-8075
Document Type: Article
Record Type: Abstract
Language: ENGLISH

Abstract: When the dorsolateral prefrontal cortex in 1 hemisphere of a rhesus monkey is **resected** 6 wk **before birth** and the **fetus survives** to postnatal ages, neurons of the corresponding cortex in the intact hemisphere issue a greatly expanded projection to the contralateral caudate nucleus in addition to a normal projection to the ipsilateral caudate. The enhancement of the crossed prefronto-caudate pathway after prenatal neurosurgery provides direct evidence for lesion-induced neuronal rearrangment in the primate telencephalon.

14/7/84 (Item 4 from file: 144) **Links**
Fulltext available through: STIC Full Text Retrieval Options
Pascal

11555383 PASCAL No.: 94-0438300

Embryo survival after prononuclear microinjection and trophectoderm biopsy

BURWINKEL T H; HAK-NAM KIM; BUSTER J E; MINHAS B S; CARSON S A

Univ. Tennessee, dep. obstetrics gynecology, Memphis TN 38163, USA
Journal: American journal of obstetrics and gynecology

, 1994, 170 (4
) 1199-1203
ISSN: 0002-9378 CODEN: AJOGAH Availability: INIST-3053;
354000045250600360
No. of Refs.: 25 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
OBJECTIVE: Our purpose was to compare murine embryo development after pronuclear microinjection of a gene construct, followed by trophectoderm biopsy at the blastocyst state, with development after a single micromanipulation, and wirth cultured controls. STUDY DESIGN: alpha -Myosin heavy-chain gene sequence was microinjected into the murine embryo pronucleus and cultured to blastocyst. After trophectoderm **biopsy** the **embryos** were allowed to reexpand. Reexpanded embryos were transferred to pseudopregnant females; implantation and live birth rates were recorded. In this study group the rates were compared with three control groups of embryos simultaneously cultured after (1) pronuclear microinjection only, (2) trophectoderm biopsy only, and (3) nonmicromanipulated, culture only

?

32/7/5 (Item 5 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

17472984 **PMID:** 17208551
Fetal intervention for mass lesions and hydrops improves outcome: a 15-year experience.

Grethel Erich J; Wagner Amy J; Clifton Matthew S; Cortes Raul A; Farmer Diana L; Harrison Michael R; Nobuhara Kerilyn K; Lee Hanmin
Division of Pediatric Surgery, Fetal Treatment Center, University of California, San Francisco, San Francisco, CA 94143-0570, USA. grethele@surgery.ucsf.edu
Journal of pediatric surgery (United States) Jan 2007 , 42 (1) p117-23 , **ISSN:** 1531-5037--Electronic **Journal Code:** 0052631
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
PURPOSE: The natural history of certain **prenatally** diagnosed masses is well known. Large thoracic mass lesions can evolve one of 2 ways, either to regress and cause minimal morbidity, or to progress and enlarge, often resulting in hydropic changes in the fetus. This nonimmune hydrops carries a dismal prognosis, with nearly all fetuses expiring before or shortly after birth. However, hydrops associated with fetal mass lesions can be halted and even

reversed with fetal intervention and treatment of the underlying defect. We examined our patients with **fetal mass** lesions to evaluate **survival** after intervention. METHODS: Institutional approval was **obtained** by the Committee on Human Research. A retrospective review was performed of 294 fetuses evaluated over 15 years with large mass lesions. All patients were evaluated for evidence of fetal hydrops using ultrasound criteria. Patients were divided according to type of intervention. Primary outcome measure was 30-day survival after birth. RESULTS: (1) Patients without fetal hydrops did not undergo **fetal** intervention and **survived** to 30 days after birth (167/172, 97%). (2) Patients with fetal mass lesions that developed hydrops fared poorly with no intervention (1/33 **survival**, 3%), whereas **fetuses** undergoing **prenatal** intervention fared much better (15/30 open, 50%; 3/10 percutaneous, 30%). (3) Four patients with hydropic congenital cystic adenomatoid malformation (n = 3) or pulmonary sequestration (n = 1) received steroids in preparation for surgery but underwent no intervention, and the patients **survived** the neonatal period. CONCLUSION: **Fetuses** with **prenatal** diagnoses of masses not associated with hydrops have excellent prognosis with survival higher than 95%. Nonimmune hydrops associated with **prenatal** diagnosis of a **fetal mass** is a devastating complication with less than 5% survival. Open **resection** of a mass causing hydrops resulted in 50% survival, with reversal of hydrops in a group with near-uniform fatality. Further investigation is warranted regarding the use of minimally invasive **prenatal** therapies including steroid administration for hydropic fetuses.
Record Date Created: 20070108
Record Date Completed: 20070205

32/7/20 (Item 20 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

15405880 **PMID:** 14533890
Management of fetal lung lesions.

Adzick N Scott
Center for Fetal Diagnosis and Treatment, Children's Hospital of Philadelphia, 34th and Civic Center Boulevard, Philadelphia, PA 19104, USA.
Clinics in perinatology (United States) Sep 2003 , 30 (3) p481-92 , **ISSN:** 0095-5108--Print **Journal Code:** 7501306
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We have learned from **prenatal** diagnosis that there is a wide spectrum of clinical severity for fetuses that have a lung mass. Accurate prognostic information is necessary for providing appropriate management and parental counseling. If an associated life-threatening anomaly is present or if the mother is ill with the mirror syndrome, then the family might choose to terminate the pregnancy. If the fetus is not hydropic and an isolated fetal lung lesion is present, the mother is followed by serial ultrasound and arrangements are made for the best possible care after birth. Some CCAMs and many BPSs will shrink in size, so it is important to try to differentiate these lesions using **prenatal** diagnostic criteria, although this technique is not always possible. All fetuses that had fetal thoracic masses without hydrops in our series survived in the setting of maternal transport, planned delivery, and postnatal evaluation at a facility with ECMO capability. Many of the babies that had large lesions at our center required ventilatory support, and six babies needed treatment with ECMO. Our impression is that these nonhydropic fetuses that had lung masses had less lung hypoplasia and a much better prognosis than those that had diaphragmatic hernia despite a

similar degree of mediastinal shift as judged by **prenatal** sonography. In asymptomatic neonates that have a cystic lung lesion, we believe that elective resection is warranted because of the risks of infection and occult malignant transformation. Malignancies consist mainly of pleuropulmonary blastoma in infants and young children and bronchioloalveolar carcinoma in older children and adults. After confirmation of CCAM location by postnatal chest CT scan with intravenous contrast, we recommend elective resection at 1 month of age or older. This age has been chosen because anesthetic risk in babies decreases after 4 weeks of age. An experienced pediatric surgeon can safely perform a lobectomy in infants with minimal morbidity. Early resection also maximizes compensatory lung growth. In contrast, we have usually followed patients with a tiny, asymptomatic, noncystic BPS if we are confident of the diagnosis based on postnatal imaging studies. We do not favor the approach of catheterization and embolization for the treatment of larger BPS lesions. If the fetus is hydropic at presentation or if hydrops develops during serial follow-up, management depends upon the gestational age. For hydropic fetuses of greater than 32 weeks' gestation, early delivery should be considered so that the lesion can be resected ex utero, but the neonatal outcome is dismal. We recently managed two such cases using an ex utero intrapartum therapy (EXIT) strategy with **resection** of the mass during the EXIT procedure. Both **fetuses survived** and one required the use of ECMO. For hydropic fetuses of less than 32 weeks' gestation, there is now a new therapeutic option, treating the lesion before birth. (55 Refs.)
Record Date Created: 20031009
Record Date Completed: 20031106

32/7/26 (Item 26 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

14676141 **PMID:** 12077758
Fetal tissue engineering: in utero tracheal augmentation in an ovine model.

Fuchs Julie R; Terada Shinichi; Ochoa Erin R; Vacanti Joseph P; Fauza Dario O
Harvard Center for Minimally Invasive Surgery, Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA.
Journal of pediatric surgery (United States) Jul 2002 , 37 (7) p1000-6; discussion 1000-6 , **ISSN:** 1531-5037--Electronic **Journal Code:** 0052631
Publishing Model Print
Document type: Comparative Study; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND/PURPOSE: This study was aimed at comparing fetal tissue engineering with autologous free grafting in an ovine model of **in utero** tracheal repair. METHODS: Chondrocytes were isolated from both elastic and hyaline cartilage **specimens harvested** from **fetal** lambs and expanded in vitro. Cells were seeded dynamically onto biodegradable scaffolds, which then were maintained in a rotating bioreactor for 6 to 8 weeks. Constructs subsequently were implanted into fetal tracheas (n = 15), in a heterologous fashion (group I). In group II, fetuses (n = 5) received autologous free grafts of elastic cartilage harvested from the ear as tracheal implants. **In vivo** specimens were harvested for histologic analysis at different time-points postimplantation. RESULTS: In the 12 of 15 **surviving fetuses** of group I, all constructs were found to resemble normal hyaline cartilage, engraft well despite their heterologous origin, and display time-dependent epithelialization derived from the native trachea. All autologous free grafts were engrafted and epithelialized at birth, retaining histologic characteristics of elastic cartilage, but were more deformed than engineered constructs. Of the lambs allowed to reach term, 5 of 5 in the

engineered group and 4 of 5 in the free graft group could breathe spontaneously. CONCLUSIONS: (1) Tissue-engineered cartilage, as well as autologous free grafts, can be implanted successfully into the fetal trachea, resulting in engraftment and function. (2) Engineered cartilage provides enhanced structural support after implantation into the fetal trachea when compared with free grafts. **Prenatal** tracheoplasty may prove useful for the treatment of severe congenital tracheal malformations.

Record Date Created: 20020621
Record Date Completed: 20020820

32/7/46 (Item 46 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

12861658 **PMID:** 9793976
Fetal blood sampling--indication-related losses.

Antsaklis A; Daskalakis G; Papantoniou N; Michalas S
First Department of Obstetrics and Gynaecology, Athens University Medical School, Alexandra Maternity Hospital, Greece.
Prenatal diagnosis (ENGLAND) Sep 1998 , 18 (9) p934-40 , **ISSN:** 0197-3851--Print **Journal Code:** 8106540

Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The aim of this study, was to determine the fetal loss rate after fetal blood sampling (FBS) in relation to the indication. In total, 1981 FBS procedures (1878 pregnancies) were included, of which 117 were performed for the detection of congenital infection (group 1), 1437 for the detection of haemoglobinopathy (group 2), 233 for **prenatal** diagnosis with normal ultrasound findings (group 3), 121 for rapid karyotyping in cases with abnormal sonographic findings (group 4) and 73 for severe growth retardation (group 5). All the procedures were performed with a free-hand technique under **continuous** ultrasound guidance. **Pregnancy** losses occurring within two weeks of FBS were considered procedure-related losses. 343 pregnancies were terminated. Of the remaining 1535 continuing pregnancies, 73 (4.8 per cent) were lost, of which 39 (2.5 per cent) were lost within two weeks of the procedure. The procedure-related losses were 3 in 103 (2.9 per cent), 17 in 1090 (1.6 per cent), 2 in 191 (1 per cent), 11 in 84 (13.1 per cent) and 6 in 67 (8.9 per cent) in groups 1, 2, 3, 4 and 5, respectively. The differences in procedural loss between the five groups were highly significant, suggesting that the method entails a much higher risk when the fetus is structurally abnormal, or severely growth retarded. Patients should therefore be counselled before the procedure accordingly.
Record Date Created: 19990107
Record Date Completed: 19990107

32/7/47 (Item 47 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

12824512 **PMID:** 9757993
Fetal blood sampling immediately before and within 24 hours of death in monochorionic twin pregnancies complicated by single intrauterine death.

Nicolini U; Pisoni M P; Cela E; Roberts A
1st Department of Obstetrics and Gynecology, University of Milano, Clinica Mangiagalli, Milan, Italy.
American journal of obstetrics and gynecology (UNITED STATES) Sep 1998 , 179 (3 Pt 1) p800-3 , **ISSN:** 0002-9378--Print **Journal Code:** 0370476
Publishing Model Print; Comment in Am J Obstet Gynecol. 1999 Feb;180(2 Pt 1) 507-8; Comment in PMID 9988835
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
OBJECTIVE: Our goal was to investigate the mechanisms that play a role in intrauterine death in monochorionic twins and that contribute to the high perinatal mortality and morbidity in the survivors. STUDY DESIGN: In 8 monochorionic twin pregnancies complicated by the intrauterine death of a single twin, we took **samples** from 5 twin **fetuses** immediately before death and from 4 of their cotwins and also from 4 **surviving fetuses** within 24 hours after death of the cotwin. RESULTS: Four of the 5 **fetuses sampled** who subsequently died were acidemic and 3 were hypoxemic. None of these **fetuses** or their cotwins were anemic at that time. All 4 survivors **sampled** within 24 hours of the death of each cotwin had low hematocrits. CONCLUSION: Fetal anemia, probably the consequence of acute blood loss just before the time of death of the cotwin, may play a role in the high mortality and morbidity found in the surviving twin. It is unlikely that immediate delivery of the surviving twin after death could affect the outcome.
Record Date Created: 19981022
Record Date Completed: 19981022

32/7/50 (Item 50 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

12578461 **PMID:** 9473089
Videofetoscopically assisted fetal tissue engineering: bladder augmentation.

Fauza D O; Fishman S J; Mehegan K; Atala A
Harvard Center for Minimally Invasive Surgery and the Department of Surgery, Children's Hospital and Harvard Medical School, Boston, MA 02115, USA.
Journal of pediatric surgery (UNITED STATES) Jan 1998 , 33 (1) p7-12 , **ISSN:** 0022-3468--Print **Journal Code:** 0052631
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
BACKGROUND/PURPOSE: Treatment of several congenital anomalies is frequently hindered by lack of enough

tissue for surgical reconstruction in the neonatal period. Minimally invasive **harvest** of **fetal tissue**, which is then processed through **tissue** engineering techniques in vitro while **pregnancy** is allowed to **continue** so that at delivery a newborn with a **prenatally** diagnosed congenital anomaly can benefit from having autologous, expanded tissue promptly available for surgical reconstruction at birth. This concept was applied to a bladder defect. METHODS: Bladder exstrophy was surgically created in ten 90- to 95-day gestation fetal lambs, which were divided in two groups. In group I, a small **fetal** bladder **specimen** was **harvested** through a minimally invasive technique (videofetoscopy). Urothelial and smooth muscle cells were then separately cultivated and expanded in vitro for 55 to 60 days, resulting in a total of approximately 200 million cells. Seven to 10 days before delivery, the cells were seeded in two layers in a 16- to 20-cm2, 3-mm thick biodegradable polyglycolic acid polymer matrix. One to 4 days after delivery, autologous engineered tissue was used for surgical augmentation of the exstrophic bladder. In group II, no harvest was performed, and the bladder exstrophy was primarily closed after delivery. In both groups, a catheter was left inside the bladder for 3 weeks, at which time a cystogram was performed and the catheter then removed. In all animals, at 60 days, another cystogram was performed and urodynamic studies of the bladder were performed. The bladder was then removed for histological analysis. RESULTS: **Fetal survival** rate was 100%. One newborn died immediately after the implantation of the engineered bladder from an anesthetic accident. The other nine (four in group I and five in group II) survived. One of the animals from group I lost its bladder catheter prematurely and had a urinary leak detected only at the time of death. There were no other complications. The engineered bladders were more compliant ($P < .05$) and had greater capacity pressures greater than 20 mm Hg ($P < .05$) than those closed primarily. Histological analysis of the engineered tissue showed a multilayered urothelial lining on the luminal side and overlying layers of smooth muscle cells surrounded by connective tissue. CONCLUSIONS: Videofetoscopically assisted **fetal** bladder engineering may be a **viable** alternative for prompt bladder reconstruction at birth. The architecture of autologous engineered fetal bladder tissue resembles that of native bladder. This concept may prove useful for the treatment of certain human neonatal conditions such as bladder and cloacal exstrophies.
Record Date Created: 19980320
Record Date Completed: 19980320

32/7/57 (Item 57 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

11631199 **PMID:** 8606889
Trisomy 16 fetus surviving into the second trimester.

Cusick W; Bork M; Fabri B; Benn P; Rodis J F; Buttino L
Center for Human Reproduction, Division of Maternal-Fetal Medicine, Chicago, IL 60610, USA.
Prenatal diagnosis (ENGLAND) Nov 1995 , 15 (11) p1078-81 , **ISSN:** 0197-3851--Print **Journal Code:** 8106540
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
A 27-year-old gravida 4, para 3 was found to have anhydramnios at 14 weeks' gestation following a size/date discrepancy noted at her routine **prenatal** visit. A detailed ultrasound revealed multiple fetal anomalies including congenital heart defect, chest hypoplasia, and bilateral dysplastic kidneys. Karyotype revealed trisomy 16 in 15/15

cells from a **tissue specimen obtained** from the **fetal** cord insertion site following elective pregnancy termination.
Record Date Created: 19960517
Record Date Completed: 19960517

32/7/59 (Item 59 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

11520407 **PMID:** 7576172
A non-human primate model for the in utero chronic catheterization of the umbilical vein. A preliminary report.

Lemery D J; Santolaya-Forgas J; Wilson L; Bieniarz A; Warsof S L
Department of Obstetrics and Gynecology, University of Illinois at Chicago, School of Medicine, IL 60612, USA.
Fetal diagnosis and therapy (SWITZERLAND) Sep-Oct 1995 , 10 (5) p326-32 , **ISSN:** 1015-3837--Print
Journal Code: 9107463
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Short-term ultrasound-guided fetal umbilical cord catheterization in humans has been reported. However, before chronic umbilical vein catheterization is attempted in humans the technique must be tested in the non-human primate model. If the fetus was to tolerate this procedure, chronic fetal umbilical vein catheterization could be used for drug administration, parenteral fetal nutrition or to monitor the changes of hematologic parameters during and after open or endoscopic fetal surgery. In this study, 4 pregnant baboons were used to test the feasibility of ultrasound-guided umbilical vein catheterization. Although the umbilical vein was successfully catheterized in all the animals, only 1 **fetus survived** the postoperative period. The 3 immediate fetal deaths were due to a fetal intra-amniotic hemorrhage, while the most likely cause of death of the 4th animal was infection. In the **surviving fetus** and mother, blood was **sampled** once a day. Neither fetomaternal hemorrhage nor thrombosis could be documented. We conclude that ultrasound-guided transplacental umbilical vein chronic catheterization is technically difficult but feasible in the baboon model. Further studies in this model are needed to improve the catheterization technique and to monitor the extent of time that the catheter may be tolerated within the umbilical vein.
Record Date Created: 19951207
Record Date Completed: 19951207

32/7/64 (Item 64 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

10875249 **PMID:** 8305757
Prenatal diagnosis of epidermolysis bullosa: first successful trial in Asia.

Shimizu H; Onodera Y; Ikeda S; Ogawa H; Suzumori K; Nishikawa T
Department of Dermatology, Keio University School of Medicine, Tokyo, Japan.

Dermatology (Basel, Switzerland) (SWITZERLAND) 1994 , 188 (1) p46-9 , **ISSN:** 1018-8665--Print **Journal Code:** 9203244
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Prenatal diagnosis of epidermolysis bullosa (EB) using **fetal** skin **biopsy specimens** has been successfully performed in Europe and America, but this technique has not previously been attempted in Asia. For the first time in Asia, we attempted to make a **prenatal** diagnosis of EB in a high-risk **fetus** by **fetal** skin **biopsy**. A skin **biopsy** was **obtained** from the **fetus** at risk of gravis type junctional epidermolysis bullosa of Herlitz. The **biopsy specimen** was studied by electron microscopy and immunohistochemistry using various monoclonal antibodies against the epidermal basement membrane zone (BMZ). There were no ultrastructural abnormalities in the BMZ, including the hemidesmosomes. Indirect immunofluorescence showed normal expression of GB3 antigen. The **pregnancy** was **continued**, and a normal, healthy infant was born. The **prenatal** diagnosis of epidermolysis bullosa is now available in Tokyo. This clinical diagnostic service is available to families from various parts of Asia.
Record Date Created: 19940311
Record Date Completed: 19940311

32/7/66 (Item 66 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

10557050 **PMID:** 8488877
In utero fetal muscle biopsy for the diagnosis of Duchenne muscular dystrophy in a female fetus "suddenly at risk".

Evans M I; Farrell S A; Greb A; Ray P; Johnson M P; Hoffman E P
Department of Obstetrics/Gynecology, Hutzel Hospital/Wayne State University, Detroit, Michigan 48201.
American journal of medical genetics (UNITED STATES) May 15 1993 , 46 (3) p309-12 , **ISSN:** 0148-7299--Print **Journal Code:** 7708900
Publishing Model Print
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
DNA methods to diagnose Duchenne muscular dystrophy (DMD) are not always informative, and we have published previously the first instance of **in utero** muscle **biopsy** to assess dystrophin in a male fetus having the same "X" as an affected sib. We present here a female fetus with a de novo X,1 translocation with breakpoint at Xp21, detected on amniocentesis for advanced maternal age. The translocation breakpoint placed her at high risk for DMD. **In utero** muscle **biopsy** at 20 weeks of gestation produced a specimen positive for dystrophin immunofluorescence indicating a likely normal fetus. The **pregnancy** was **continued**, and at term the baby girl was found to have normal serum creatine kinase levels, and was therefore unaffected with DMD. Our experiences add de novo Xp21 translocation to the indications for **in utero** muscle **biopsy** for diagnosis of DMD.
Record Date Created: 19930610
Record Date Completed: 19930610

32/7/67 (Item 67 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

10070316 **PMID:** 1730955

In vivo magnetic resonance imaging of fetal cat neural tissue transplants in the adult cat spinal cord.

Wirth E D; Theele D P; Mareci T H; Anderson D K; Brown S A; Reier P J
Department of Neuroscience, University of Florida, Gainesville.
Journal of neurosurgery (UNITED STATES) Feb 1992 , 76 (2) p261-74 , **ISSN:** 0022-3085--Print **Journal Code:** 0253357
Contract/Grant No.: 1 PO1 NS27511-01; NS; United States NINDS; P41-RR-02278; RR; United States NCRR; T32 MH15737; MH; United States NIMH
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Magnetic resonance (MR) imaging was evaluated for its possible diagnostic application in determining the **survival** of **fetal** central nervous system tissue grafts in the injured spinal cord. Hemisection cavities were made at the T11-L1 level of eight adult female cats. Immediately thereafter, several pieces of **tissue**, either **obtained** from the **fetal** cat brain stem on **embryonic** Day 37 (E-37), from the fetal neocortex on E-37, or from the fetal spinal cord on E-23, were implanted into the cavities made in seven cats. The eighth cat served as a control for the effect of the lesion only. In another group of four animals, a static-load compression injury was made at the L-2 level. Seven weeks later, the lesion was resected in three cases and fragments of either fetal brain-stem or spinal cord tissue were introduced. A small cyst was observed in a fourth cat in the compression injury group and a suspension of dissociated E-23 brain-stem cells was injected into this region of cavitation without disturbing the surrounding leptomeninges. Five months to 2 years posttransplantation, MR imaging was performed with a 2.0-tesla VIS imaging spectrometer by acquiring multislice spin-echo images (TR 1000 msec, TE 30 msec) in both the transverse and sagittal planes. Collectively, these intermediate-weighted images revealed homogeneous, slightly hyperintense signals at the graft site relative to the neighboring host tissue in seven of the 11 graft recipients. Two of the remaining four cats exhibited signals from the graft site that were approximately isointense with the adjacent host spinal cord, and the final two cats and the lesion-only control presented with very hypointense transplant/resection regions. The hyperintense and isointense images were tentatively interpreted as representing viable graft tissue, whereas the hypointense transplant/resection sites were considered to be indicative of a lack of transplant survival or the absence of tissue in the lesion-only control animal. Postmortem gross inspection of fixed specimens and light microscopy verified the MR findings in the control animal in 10 of the 11 graft recipients by showing either transplants and/or cysts corresponding to the MR images obtained. In one cat in the hemisection group, histological analysis revealed a very small piece of graft tissue that was not detected on the MR images. Therefore, it is suggested that within certain spatial- and contrast-resolution limits, MR imaging can reliably detect the presence of transplanted neural tissue in both the hemisected and compression-injured spinal cord of living animals.(ABSTRACT TRUNCATED AT 400 WORDS)
Record Date Created: 19920218
Record Date Completed: 19920218

32/7/69 (Item 69 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09895505 **PMID:** 1833736
[Trisomy 20 mosaicism in amniotic cell culture. Genetic counselling during the prenatal diagnosis]

Trisomie 20 en mosaique dans une culture de cellules amniotiques. Conseil genetique au cours du diagnostic **prenatal**.
Rabineau D
Service d"istologie-Embryologie-Cytogenetique, Groupe hospitalier Cochin, Paris.
Presse medicale (Paris, France - 1983) (FRANCE) Sep 14 1991 , 20 (28) p1327-9 , **ISSN:** 0755-4982--Print
Journal Code: 8302490
Publishing Model Print
Document type: Case Reports; English Abstract; Journal Article
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The author presents a new case of trisomy 20 mosaicism in an amniotic fluid culture and emphasizes the special aspects of this chromosomal abnormality. The **prenatal** diagnosis of "pseudo-mosaicism" is easier when in situ culture techniques are used. Controls of the results on a new **sample** of amniotic fluid and/or on **foetal** blood are useful to reinforce the diagnosis and to allow **pregnancy** to be **continued**.
Record Date Created: 19911030
Record Date Completed: 19911030

32/7/71 (Item 71 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09613212 **PMID:** 2149678
First trimester prenatal diagnosis of Tay-Sachs disease using the sulfated synthetic substrate for hexosaminidase A.

Callahan J W; Archibald A; Skomorowski M A; Shuman C; Clarke J T
Division of Clinical Genetics, Hospital for Sick Children.
Clinical biochemistry (CANADA) Dec 1990 , 23 (6) p533-6 , **ISSN:** 0009-9120--Print **Journal Code:** 0133660
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Uncultured and cultured **embryonic** trophoblastic **tissue obtained** by chorionic villus **sampling** (CVS) displays enzyme activity towards 4-methylumbelliferyl-2-acetamido-2-deoxy-beta-D-glucopyranosyl-6-sulfate (MUGS), a

specific substrate for Hexosaminidase A (Hex A), the enzyme deficient in Tay-Sachs disease (TSD). Specific activity is comparable to that found in cultured amniocytes and fibroblasts. The enzyme activity has a pH optimum of 4.1 and an apparent Km of 6 x 10(-4) mol/L. Thirteen pregnancies in eight families at risk for TSD were monitored by CVS using MUGS as the Hex A substrate. Four fetuses were proven affected by enzyme analysis of **fetal tissues** and cultured **fetal** fibroblasts **obtained** at the time of termination of the pregnancies. Nine **fetuses** were judged to be unaffected. Eight babies were clinically normal while the other **pregnancy** is **continuing**. The use of MUGS as substrate for Hex A makes **prenatal** diagnosis by CVS of families at risk for TSD simple, direct and accurate.
Record Date Created: 19910329
Record Date Completed: 19910329

32/7/72 (Item 72 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09608868 **PMID:** 2286031
Duchenne and Becker muscular dystrophies: genetics, prenatal diagnosis, and future prospects.

Bieber F R; Hoffman E P
Department of Pathology, Harvard Medical School, Boston, Massachusetts.
Clinics in perinatology (UNITED STATES) Dec 1990 , 17 (4) p845-65 , **ISSN:** 0095-5108--Print **Journal Code:** 7501306
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
DMD and BMD are now understood at the genetic, biochemical, and molecular levels. At the genetic level, both disorders result from mutations of the X-linked gene encoding dystrophin. At the biochemical level, DMD results from the deficiency of a large protein called dystrophin, whereas BMD results when dystrophin is present, though abnormal in either amount or molecular structure. To date, thousands of patients have been analyzed for mutations of the dystrophin gene in peripheral blood DNA or alterations of the dystrophin protein in muscle tissue. The severity of the clinical phenotype of these patients has been compared with their dystrophin gene mutations and corresponding dystrophin protein alterations, revealing an unexpectedly high degree of correlation. Thus, information derived from the molecular analysis (DNA or protein) of a particular patient provides a "molecular diagnosis," which is highly predictive of the clinical course that patient can be expected to follow. Because molecular diagnoses are independent of the patient's age, they provide a prognosis for the large majority of muscular dystrophy patients even before clinical symptoms of their disease become apparent. Such prognostic molecular diagnoses have proven particularly valuable when the patient is an isolated case, with no family history for the disorder. Prenatal genetic diagnosis of DMD or BMD may involve use of Southern blot or PCR techniques to search for a deletion in the DNA of at-risk fetuses or more complicated family linkage studies using intragenic and flanking RFLPs. More recently, assay of dystrophin content in fetal skeletal or cardiac muscle from at-risk abortuses has been accomplished, allowing definitive discrimination of affected and normal fetuses in cases in which deletion analyses and family DNA studies were equivocal. **In** utero **fetal** skeletal muscle **biopsy** for dystrophin protein assay has actually been accomplished in at least one at-risk pregnancy in which family DNA studies were uninformative. Dystrophin was present in skeletal muscle from this 20-week-old male fetus, and the **pregnancy continued**,

resulting in the term birth of a healthy male infant. The future holds exciting opportunities for neonatal screening and treatment of these devastating neuromuscular diseases. (53 Refs.)
Record Date Created: 19910326
Record Date Completed: 19910326

32/7/74 (Item 74 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09521559 **PMID:** 2121301
New approaches in the treatment of haemolytic disease of the fetus.

Tannirandorn Y; Rodeck C H
Bailliere's clinical haematology (ENGLAND) Apr 1990 , 3 (2) p289-320 , **ISSN:** 0950-3536--Print **Journal Code:** 8800474
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The incidence of Rh haemolytic disease of the fetus and newborn complicating pregnancy has fallen since the implementation of prophylaxis with Rh immune globulin. However, occasional mismatched blood transfusions and ineffective or inadequate prophylaxis still result in a few Rh-alloimmunized patients requiring treatment during pregnancy. The development of a safe technique for **obtaining** pure **fetal** blood **samples** has provided the opportunity to assess correctly the severity of anaemia and to study fetal haematology and biochemical parameters, and hence to gain a better understanding of the pathophysiology of this condition. The aim of antenatal management is to predict whether or not the fetus is severely affected, to correct fetal anaemia and to deliver the baby at the optimal time. Fetal IVT is the standard treatment in severe Rh alloimmunization in many centres. However, high volume transfusion without overloading the fetal circulation, as well as increasing the interval between transfusions without jeopardizing the fetal condition, can be achieved by a combination of IVT and IPT. Thus, the total number of transfusions needed and the overall procedure-related risk for each fetus is reduced. With the recent advances in **fetal** medicine, haematology and neonatology, the **survival** rate of affected **fetuses** in some centres is now about 90%. Fetal death will continue to be associated with two sets of circumstances: trauma or complications due to IVT or IPT in early gestation when delivery is not feasible, and late referrals with such severe hydrops that its reversal is not possible. There is still, therefore, a need for research into new methods of treatment, such as high dose intravenous IgG, which can non-invasively diminish fetal red cell destruction. (98 Refs.)
Record Date Created: 19901212
Record Date Completed: 19901212

32/7/75 (Item 75 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

09509552 **PMID:** 2215441
Prenatal diagnosis and congenital disease: role of the clinical nurse specialist.

Lemons P K; Brock M J
Neonatal network - NN (UNITED STATES) Oct 1990 , 9 (3) p15-22 , **ISSN:** 0730-0832--Print **Journal Code:** 8503921
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Birth defects reflect the infant's genetic constitution and are generally divided into four major categories: multifactorial, single-gene, chromosomal, and environmental. The etiology of the specific disorder is directly related to its risk of occurrence/recurrence, which can be theoretically or specifically calculated. Suspicion of genetic disease in an unborn child is heightened by a history of disease in blood relatives and by the presence of multiple miscarriages and/or increased maternal age. Current **prenatal** screening tools include maternal/**fetal sampling** (**tissue**, cells, amniotic fluid) and **fetal** visualization. All these tests have specific complications and limitations. Families undergoing **prenatal** testing are likely to experience anxiety, which may **continue** throughout the **pregnancy** despite a diagnosis of an unaffected fetus. Such anxiety can interfere with attachment to the unborn child. The aware clinical nurse specialist is in a position to help all parents by providing clear and accurate information, sensitive emotional support, and by optimizing social support systems.
Record Date Created: 19901120
Record Date Completed: 19901120

32/7/78 (Item 78 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

08990248 **PMID:** 2721460
Circadian rhythm of vasopressin levels in cerebrospinal fluid of the fetus: effect of continuous light.

Stark R I; Daniel S S
Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, New York 10032.
Endocrinology (UNITED STATES) Jun 1989 , 124 (6) p3095-101 , **ISSN:** 0013-7227--Print **Journal Code:** 0375040
Contract/Grant No.: 13063; United States PHS
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We have measured the concentrations of vasopressin in sequential **samples** of cerebrospinal fluid (CSF) **obtained** from **fetal** lambs between 108 and 130 days gestation. There was a clear and significant ($F = 4.46$; P less than 0.005) rhythm in vasopressin concentrations in the CSF of nine fetuses, characterized by a mean trough value of 19.4 +/- 6.4 pg/ml (mean +/- SD) at 0200 h and a peak value of 41.1 +/- 28.0 pg/ml at 1400 h. The mean cycle length was 23.2 +/- 1.7 h, with the majority (greater than 80%) of peak concentrations found during daylight hours. There were no concurrent fluctuations in concentrations of vasopressin in plasma or Na, K, Cl, or osmolality in CSF. To examine the relationship between environmental cycles of light and darkness and rhythm of vasopressin

concentrations in CSF, **pregnant** animals were **maintained** in a constant light environment. In the five fetuses of ewes maintained under these conditions, the rhythm of vasopressin in CSF was markedly damped or not apparent (F = 1.50; P greater than 0.15). These results demonstrate that prominent circadian rhythm of vasopressin in the CSF of the fetus **in utero**. Despite the fact that the fetus is sequestered from direct influences of the environment, exposure of the pregnant ewe to constant light disrupts the fetal pacemaker that generates the circadian rhythm of vasopressin in CSF. Studies of this rhythm in the fetal lamb, therefore, provide a means to examine the mechanisms of entrainment and assess **prenatal** influences on circadian organization of the fetus.
Record Date Created: 19890628
Record Date Completed: 19890628

32/7/79 (Item 79 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

08981336 **PMID:** 2716956
Role of steroid 5 alpha-reductase activity in sexual differentiation of the guinea pig.

Connolly P B; Resko J A
Department of Physiology, School of Medicine, Oregon Health Sciences University, Portland.
Neuroendocrinology (SWITZERLAND) Mar 1989 , 49 (3) p324-30 , **ISSN:** 0028-3835--Print **Journal Code:** 0035665
Contract/Grant No.: HD-07133; HD; United States NICHD; HD-16022; HD; United States NICHD; RR-00163; RR; United States NCRR
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The possible role of 5 alpha-reduction of steroids in the sexual differentiation of guinea pigs was determined by treating pregnant guinea pigs with a 5 alpha-reductase activity (5 alpha RA) inhibitor (17 beta-N,N-diethylcarbamoyl-4-methyl-4-aza-5 alpha-androstan-3-one, 4MA, 10 mg/day) from day 30 to 55 of gestation. 5 alpha RA in **fetal** diencephalon **tissue obtained** from 4MA-treated mothers on day 55 of gestation was suppressed compared to that of control tissue. Four litters receiving 4MA were **carried** to **term** along with an equal number of litters receiving the vehicle alone. Males that received 4MA **in utero** (n = 6) had altered external genitalia, i.e., hypospadias and reduced anogenital distances, but their adult copulatory behavior did not differ from that of controls (n = 7). In order to evaluate treatment effects on the hypothalamic-pituitary axis, all animals were challenged with estradiol benzoate (EB, 10 micrograms in oil, s.c.) 2 weeks after gonadectomy. Serial plasma samples were obtained and analyzed for luteinizing hormone (LH) using an heterologous radioimmunoassay. Control females (n = 13) and 4MA-treated females (n = 5) released LH in surge quantities about 42 h after EB treatment. Plasma from 4MA-treated females differed from controls in that it contained greater overall quantities of LH (p less than 0.05) and greater amounts at the time of the LH surge (p less than 0.05). Regardless of treatment males did not respond to EB.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19890619
Record Date Completed: 19890619

32/7/81 (Item 81 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

08770025 **PMID:** 3192951

The expression of congenital ichthyosiform erythroderma in second trimester fetuses of the same family: morphologic and biochemical studies.

Holbrook K A; Dale B A; Williams M L; Perry T B; Hoff M S; Hamilton E F; Fisher C; Senikas V
Department of Biological Structure, University of Washington School of Medicine, Seattle 98195.
Journal of investigative dermatology (UNITED STATES) Dec 1988 , 91 (6) p521-31 , **ISSN:** 0022-202X--Print
Journal Code: 0426720
Contract/Grant No.: AR 21557; AR; United States NIAMS; DE 04660; DE; United States NIDCR; HD 17664; HD; United States NICHD
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The first born offspring of first-cousin parents was affected with a keratinization disorder thought to be nonbullous congenital ichthyosiform erythroderma (CIE). In each of three subsequent pregnancies, the parents elected to have **prenatal** diagnosis based on evaluation of fetal skin biopsies. The epidermis of fetus 1 was identical to normal 21-wk estimated gestation age (EGA) fetal epidermis, but because keratinization begins normally around 24 wk EGA, the procedure was repeated 4 wk later. A thin epidermis with a few layers of stratum corneum indicated a normal **fetus** and a healthy infant was born at term. Skin **biopsy samples** from **fetus** 2 gave conflicting results; the epidermis of one **sample** appeared normal but the second had 5-15 layers of incompletely keratinized cells superficial to basal and intermediate layers. The hair canals of both samples were hyperkeratotic. Pelleted amniotic fluid cells contained aggregates of incompletely keratinized epidermal cells and concentric rings of keratinized cells. The fetus was thought to be affected and the pregnancy terminated. Regional variation in epidermal thickness and keratinization was noted upon gross examination of the fetus and by histology of the skin. Marked hyperkeratinization of follicles was evident in all regions. No abnormal keratins were expressed in the affected epidermis but epidermal lipids analyzed from two body regions had a lower triglyceride content and a higher content of free sterols compared with age-matched, normal fetal epidermis. Immunolabeling for markers of differentiation revealed variable stages of epidermal differentiation according to region. Four structurally identical **biopsy samples** were **obtained** from a third **fetus** . The epidermis appeared normal for age and hair canals were keratinized to various extents. The **pregnancy** was **continued** and at 33 wk a male infant was born with a severe ichthyosis of the face and scalp and fine, white scaling on the body. The epidermis of both the severely and mildly affected regions of the newborn had a thick, compact stratum corneum and other features of CIE. Scars from all four fetal biopsies were identified on the trunk, in areas which appeared less affected clinically. This study reports, for the first time, the criteria for **prenatal** diagnosis of CIE and the variable expression of this disorder in the midtrimester fetus. More importantly, it demonstrates the risks and pitfalls of this **in utero** diagnosis based on epidermal morphology.
Record Date Created: 19890111
Record Date Completed: 19890111

32/7/82 (Item 82 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options

MEDLINE(R)

08719572 **PMID:** 3048478
In utero bone marrow transplantation of fetal baboons with mismatched adult marrow: initial observations.

Roodman G D; Vandeberg J L; Kuehl T J
Research Service, Audie L. Murphy VA Hospital, San Antonio, TX 78284.
Bone marrow transplantation (ENGLAND) Mar 1988 , 3 (2) p141-7 , **ISSN:** 0268-3369--Print **Journal Code:** 8702459
Contract/Grant No.: HL-31264; HL; United States NHLBI
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Recent advances in **prenatal** diagnoses of sickle cell anemia and thalassemia permit early identification of affected fetuses. However, the only intervention possible to date is abortion of the affected fetuses. Transplantation of normal marrow into fetuses **in utero** could correct these life-threatening disorders, but to accomplish this techniques must be developed for fetal transplantation in man. Therefore, we have transplanted fetal baboons with mismatched adult baboon bone marrow from donors that differed at the glucose phosphate isomerase locus. Twenty-two fetuses between 60 and 160 days of gestation (term gestation is 182 days) were transplanted intraperitoneally with 10(9) marrow mononuclear cells/kg body weight using an ultrasonic technique. No immunosuppressive or preparative regimen was given prior to or after transplantation, and all **fetuses** tolerated the procedure well. One month after transplantation **fetal** blood **samples** were **obtained** to assess chimerism. Three chimeras were detected among 10 **fetuses** transplanted at 80 days' gestation, and no chimeras were detected in fetuses greater than 80 days' gestation at the time of transplantation. All chimeras died **in utero** during the third trimester of pregnancy: one of an intrauterine infection at 160 days' gestation, one at 135 days' gestation and one at 145 days' gestation. In contrast, the other 19 non-chimeric **fetuses survived**. These data suggest: (1) **in utero** fetal bone marrow transplantation is technically feasible in primates; (2) that allogeneic adult bone marrow can engraft and persist for at least 1 month in fetal baboons transplanted at 80 days of gestation; and (3) that delineation of the causes for loss of fetal chimeras should prove valuable in assessing the therapeutic potential for **in utero** bone marrow transplantation in man.
Record Date Created: 19881107
Record Date Completed: 19881107

32/7/84 (Item 84 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

08365727 **PMID:** 3307426
The nonpredictive value of fetal urinary electrolytes: preliminary report of outcomes and correlations with pathologic diagnosis.

Wilkins I A; Chitkara U; Lynch L; Goldberg J D; Mehalek K E; Berkowitz R L
American journal of obstetrics and gynecology (UNITED STATES) Sep 1987 , 157 (3) p694-8 , **ISSN:** 0002-9378--Print **Journal Code:** 0370476
Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Fetal urine was **sampled** 12 times in nine **fetuses** with sonographically diagnosed urinary tract obstruction to assess renal function. By previously proposed criteria, four fetuses were predicted to have poor renal function. Two of these fetuses were found to have renal dysplasia on autopsy after elective termination. The other two died in the neonatal period but only one of these had histologic evidence of renal dysplasia. Five fetuses were predicted to have good renal function. Three of these developed renal failure after birth, one was found to have renal dysplasia on autopsy after elective termination, and one is **alive** and well. We conclude that **fetal** urine electrolytes are not necessarily an accurate predictor of neonatal renal function.
Record Date Created: 19871022
Record Date Completed: 19871022

32/7/85 (Item 85 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

08229915 **PMID:** 3559324
[Fetal blood sampling by liver puncture]

Koresawa M; Inaba J; Iwasaki H
Nippon Sanka Fujinka Gakkai zasshi (JAPAN) Mar 1987 , 39 (3) p395-9 , **ISSN:** 0300-9165--Print **Journal Code:** 7505749
Publishing Model Print
Document type: English Abstract; Journal Article
Languages: JAPANESE
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Fetal blood sampling has been performed in several ways; placentacentesis, fetoscopy, or umbilical code puncture. The problems with these methods are technical difficulties and contamination of maternal blood or amniotic fluid. To solve these problems, we have tried fetal blood sampling by fetal liver puncture with a 21 approximately 23 gauge needle through the maternal abdomen under real time scan guidance. 10 patients underwent this procedure. They ranged from 18 weeks to 22 weeks of gestation at the time of sampling. The sampling procedures were done easily and the **samples** taken were shown to be pure **fetal** blood by red blood cell sizing. All the patients **continued pregnancy** after the examination and none of the pregnancies was influenced by the puncture. 7 patients have been delivered with neither sampling scars nor damage to liver function. This method provides pure fetal blood, the procedure is simple and, in our experience, no complications have occurred.
Record Date Created: 19870520
Record Date Completed: 19870520

32/7/90 (Item 90 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

07633634 **PMID:** 4004478
[Prenatal diagnosis of severe hereditary immunologic deficiencies]

Diagnostic antenatal des deficits immunitaires hereditaires graves.
Durandy A; Dumez Y; Griscelli C
Archives francaises de pediatrie (FRANCE) Mar 1985 , 42 (3) p163-7 , **ISSN:** 0003-9764--Print **Journal Code:** 0372421
Publishing Model Print
Document type: English Abstract; Journal Article
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The recent progress in antenatal diagnosis methods led us to develop the antenatal diagnosis of several forms of hereditary and severe immune deficiencies (ID): severe combined ID (13 cases), combined ID associated with a defective expression of HLA (2 cases), X-linked agammaglobulinemia (4 cases), chronic granulomatous disease (1 case). Antenatal diagnosis was performed by studying by micromethods lymphocyte markers and functions in **fetal** venous blood **samples obtained** under foetoscopy (20 cases) or echography (1 case). Cytological studies were coupled with microscopical examination of the skin and the hair of a foetus at risk for a Chediak-Higashi disease. These methods allowed the **continuation** of the **pregnancy** in 16 cases. Thirteen neonates were normal and two pregnancies go on. In one case, the diagnosis of the integrity of the immune system led to the birth of a child suffering from a severe combined ID not yet described. This child was cured with a HLA semi-identical bone-marrow transplantation. An abortion was proposed for two fetuses affected with severe combined ID which was confirmed by histological examination. Two accidental abortions occurred, one of them probably as a consequence of the fetoscopy.
Record Date Created: 19850723
Record Date Completed: 19850723

32/7/92 (Item 92 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

07485759 **PMID:** 6517057
DNA analysis of first-trimester chorionic villous biopsies: test for maternal contamination.

de Martinville B; Blakemore K J; Mahoney M J; Francke U
American journal of human genetics (UNITED STATES) Nov 1984 , 36 (6) p1357-68 , **ISSN:** 0002-9297--Print **Journal Code:** 0370475
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We investigated the reliability of chorionic villous biopsy as a method to **obtain tissues** reflecting the genetic constitution of the **embryo**. In 12 pregnancies before elective termination, we searched for detectable maternal tissue after careful dissection of villi from small 2-5-mg specimens that yielded 7 micrograms of DNA per mg tissue. In Southern blotting experiments (1-2 micrograms DNA per lane), restriction fragment length polymorphisms

(RFLPs) at an autosomal (D14S1) and a sex chromosomal (DXYS1) locus allowed recognition of maternally and embryonically derived alleles. Pure villi were obtained in six of the seven informative cases. One biopsy was not dissected satisfactorily; a mixture of embryonic and maternal DNA was found. Nonvillous tissues were mostly maternally derived in eight informative cases. Sex determination by molecular analysis (alleles at the DXYS1 locus) agreed with the karyotypes of uncultured or cultured villi. In one **continuing pregnancy**, distinct RFLPs indicated maternal inheritance of the alpha-thalassemia 1 trait in a female embryo without detectable maternal contamination. Reliable **prenatal** diagnosis depends on the specimen's purity. Maternal contamination can be evaluated by DNA analyses.
Record Date Created: 19850204
Record Date Completed: 19850204

32/7/94 (Item 94 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

07077986 **PMID:** 6310398
Prenatal diagnosis of sickle-cell anemia in the first trimester of pregnancy.

Goossens M; Dumez Y; Kaplan L; Lupker M; Chabret C; Henrion R; Rosa J
New England journal of medicine (UNITED STATES) Oct 6 1983 , 309 (14) p831-3 , **ISSN:** 0028-4793--Print
Journal Code: 0255562
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
To investigate the usefulness of chorionic **biopsy** for **prenatal** diagnosis of sickle-cell anemia by restriction-endonuclease analysis of fetal DNA, we studied 30 pregnancies before elective abortion. When the reproducibility of the technique for **obtaining** adequate DNA **samples** was established, we successfully applied the test to five pregnancies at risk for sickle-cell anemia. In two cases, sickle-cell disease of the fetus led to a decision to terminate the pregnancy. In three other cases, a normal or AS genotype was demonstrated. One normal infant has been born, and one other **pregnancy** is **continuing** normally. In one case in which fetal death was observed three weeks after sampling, placental abnormalities found on histologic examination were compatible with a chromosomal aberration. Our study shows that chorionic **biopsy** is feasible for the **prenatal** diagnosis of sickle-cell disease before the 10th gestational week. If subsequent experience demonstrates this technique to be safe enough for mother and fetus, the ability to test in early pregnancy may make prenatal diagnosis acceptable to more couples at risk for serious genetic disorders.
Record Date Created: 19831021
Record Date Completed: 19831021

32/7/95 (Item 95 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

06964853 **PMID:** 6187867

Epidermolytic hyperkeratosis: ultrastructure and biochemistry of skin and amniotic fluid cells from two affected fetuses and a newborn infant.

Holbrook K A; Dale B A; Sybert V P; Sagebiel R W
Journal of investigative dermatology (UNITED STATES) Apr 1983 , 80 (4) p222-7 , **ISSN:** 0022-202X--Print
Journal Code: 0426720
Contract/Grant No.: AM 21557; AM; United States NIADDK; DE 04660; DE; United States NIDCR
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Skin biopsy samples and amniotic fluid cells **obtained in utero** from two **fetuses** at risk for epidermolytic hyperkeratosis were examined by light and electron microscopy. Both fetuses were affected; the second was **carried** to **term**. Epidermal extracts were prepared from blisters of the newborn for analysis of keratin and filaggrin proteins. Abnormal clumps of keratin filaments were present in all layers of the prekeratinized fetal epidermis except the periderm and stratum germinativum. A significant population of amniotic fluid cells also contained the filament aggregations. **Prenatal** diagnosis of the disease should be possible using cells **obtained** at amniocentesis, thus avoiding **fetal** skin **biopsy**. Biochemical studies showed abnormalities in keratin and filaggrin proteins. The structural alterations in the tissue might be a consequence of altered interaction between these two abnormal epidermal proteins.
Record Date Created: 19830505
Record Date Completed: 19830505

32/7/96 (Item 96 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

06391867 **PMID:** 6110859
Direct intravascular fetal blood transfusion by fetoscopy in severe Rhesus isoimmunisation.

Rodeck C H; Kemp J R; Holman C A; Whitmore D N; Karnicki J; Austin M A
Lancet (ENGLAND) Mar 21 1981 , 1 (8221) p625-7 , **ISSN:** 0140-6736--Print **Journal Code:** 2985213R
Publishing Model Print
Document type: Case Reports; Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Two fetuses with severe anaemia due to rhesus incompatibility each received two early blood transfusions (between 23 and 25 weeks) by fetoscopy. The blood was given directly into an umbilical vessel, either at the umbilicus or at the placental cord insertion. **Fetal** blood **samples** were taken before and after transfusion to assess the haematological status of the **fetus**. One grossly hydropic **fetus survived**.
Record Date Created: 19810528
Record Date Completed: 19810528

32/7/97 (Item 97 from file: 155) **Links**
Fulltext available through: STIC Full Text Retrieval Options
MEDLINE(R)

06126173 **PMID:** 7189095
In utero paternity testing utilizing fetal blood obtained by midtrimester fetoscopy.

Golbus M S; Stephens J D; Cann H M
American journal of human genetics (UNITED STATES) Jan 1980 , 32 (1) p88-91 , **ISSN:** 0002-9297--Print
Journal Code: 0370475
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
To evaluate paternity in a case where both rape and conjugal coitus had occurred close to the time of conception, fetoscopy with **fetal** blood **sampling** was performed at 20 weeks gestation. Detailed blood group typing of the wife, husband, and fetus, and the presence of a very long Y chromosome in the last two, indicated a 99.9% chance that the fetus was fathered by the husband and only a 0.1% chance that it was fathered by "some other male Caucasian." The couple elected to **continue** the **pregnancy**. Neonatal testing verified the prenatal findings.
Record Date Created: 19800523
Record Date Completed: 19800523

32/7/108 (Item 11 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0077157901 **EMBASE No:** 1998066374
Videofetoscopically assisted fetal tissue engineering: Skin replacement

Fauza D.O.; Fishman S.J.; Mehegan K.; Atala A. // Atala A.
Harvard Ctr. Minimally Invasive S., Departments of Surgery and Urology, Children's Hosp. Harvard Med. Sch., Boston, MA, United States // Children's Hospital, Hunnewell 3, 300 Longwood Ave, Boston, MA 02115, United States
Corresp. Author: Atala A.
Corresp. Author Affil: Children's Hospital, 300 Longwood Ave, Boston, MA 02115, United States

Journal of Pediatric Surgery (J. Pediatr. Surg.) (United States) February 1, 1998 , 33/2 (357-361)
CODEN: JPDSA **ISSN:** 00223468
Document Type: Journal ; Conference Paper **Record Type:** Abstract
Language: English **Summary language:** English
Number of References: 27

Background/Purpose: Treatment of several congenital anomalies is frequently hindered by lack of enough tissue for surgical reconstruction in the neonatal period. The purposes of this study were (1) introduction of a novel concept in perinatal surgery, involving minimally invasive **harvest** of **fetal tissue**, which is then processed through **tissue**

engineering techniques in vitro while **pregnancy** is allowed to **continue**, so that, at delivery, the newborn can benefit from having autologous, expanded tissue promptly available for surgical implantation at birth; (2) analysis of the progress of an engineered fetal skin graft with time, after implantation in the neonate; and (3) study of the effects of current tissue engineering techniques on fetal keratinocytes and fetal dermal fibroblasts. Methods: Ten 90- to 95-day-gestation **fetal** lambs underwent surgical creation of two large paramedian **excisional** skin defects on the posterior body wall. Subsequently, **fetal** skin **specimens** no larger than 1.5 x 1.5 cm were videofetoscopically harvested. Fetal keratinocytes and dermal fibroblasts were then separately cultivated and expanded in vitro for 45 to 50 days, resulting in a total of approximately 250 to 300 million cells. Seven to 10 days before fetal delivery, all cells were seeded in two layers on a 16 to 20-cm SUP 2, 3-mm thick biodegradable polyglycolic acid polymer matrix. One to 4 days after delivery, the autologous engineered skin was implanted over one of two previously created skin defects. The second skin defect region received an absorbable polymer scaffold without cells as a control. If necessary, the original skin wounds were further amplified before implantation. Each animal provided at least one time-point for histological analysis of both types of repair through excisional biopsies performed at weekly intervals, up to 8 weeks postimplantation. Normal skin specimens were also used as controls. Results: **Fetal** and neonatal **survival** rates were 100%. Based on previous postnatal skin engineering studies, fetal dermal fibroblasts multiplied significantly faster in vitro (approximately fivefold) than expected. Fetal keratinocytes multiplied at expected postnatal rates. The engineered grafts induced faster epithelization of the wound (partial at 1 week and complete between 2 and 3 weeks postoperatively) than did the acellular ones (partial at 3 weeks and complete between 3 and 4 weeks postoperatively) Analysis of skin architecture showed a higher level of epidermal organization and less dermal scarring in the wounds that received the engineered, cell-implanted polymer scaffold. Conclusions: (1) Videofetoscopically assisted **fetal tissue** engineering is a **viable** method for **obtaining** expanded autologous **tissue** for prompt surgical reconstruction at birth. (2) **Fetal** skin can be expanded and engineered in vitro at faster rates than expected postnatally, with current tissue engineering techniques. (3) Engineered autologous fetal skin induces a faster and more organized healing of neonatal skin defects than that observed with second intention. This concept may prove useful for the treatment of certain human neonatal conditions such as giant neoplasias, ectopia cordis, and other body wall defects.

32/7/109 (Item 12 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options

0076795625 **EMBASE No:** 1997088596

Screening for congenital toxoplasmosis: Pregnancy outcome after antenatal diagnosis in a series of 211 cases

Depistage de la toxoplasmose congenitale: Devenir des grossesses apres le diagnostic antenatal. A propos de 211 cas

Abboud P.; Bednarczyk L.; Quereux C. // Villena I.; Chemla C.; Pinon J.M. // Leroux B. // Talmuld M.
Serv. de Gynecol.-Obstetrique, Groupe Toxoplasmose, Hopital Maison Blanche, 45, rue Cognacq-Jay, F 51100 Reims, France // Laboratoire de Parasitologie, Groupe Toxoplasmose, Hopital Maison Blanche, 45, rue Cognacq-Jay, F 51100 Reims, France // Service de Pediatrie B, CHU de Reims, American Memorial Hospital, rue Cognacq-Jay, F 51100 Reims, France // Service d'Ophtalmologie, CHU de Reims, Hopital Robert-Debre, F 51100 Reims, France
Corresp. Author: Quereux C.
Corresp. Author Affil: Service de Gynecologie-Obstetrique, CHU, Hopital Maison Blanche, 45, Rue Cognacq-Jay, F 51100 Reims, France

Journal de Gynecologie Obstetrique et Biologie de la Reproduction (J. GYNECOL. OBSTET. BIOL. REPROD.) (France) May 1, 1997 , 26/1 (40-46)
CODEN: JGOBA **ISSN:** 03682315
Document Type: Journal ; Article **Record Type:** Abstract
Language: French **Summary language:** French; English
Number of References: 17

Objective. To emphasize the importance of follow-up after birth of infants with an antenatal diagnosis of congenital toxoplasmosis. Methods. Retrospective study from July 1987 through January 31 1995 on 211 women (214 fetuses) who had undergone ovular biopsy for toxoplasmosis seroconversion during pregnancy. Results. Antenatal diagnosis was positive in 13 patients (6.2%). Four pregnancies were terminated during the second trimester. Delivery was triggered at 37 weeks gestation in one woman and in 8 others **pregnancy** was **continued** with Fansidar(R). All infants were born **live** with infraclinic disease. Two **fetal** deaths related to biopsy technique occurred (0.95%) and one pregnancy was terminated before the results had been obtained. Only 21.3% of the patients were delivered in our unit. A total of 197 infants were delivered wit a negative antenatal diagnosis: 93 were healthy, 5 had congenital toxoplasmosis, 1 died at 3 months and 98 had no or incomplete follow-up. Conclusion. Incomplete post-natal follow-up is in contraindication with the excellent performance of antenatal diagnosis of congenital toxoplasmosis. Greater care is needed, especially since now only an amniocentesis is required to detect the parasite genome with polymerase chain reaction.

32/7/110 (Item 13 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options

0076645973 **EMBASE No:** 1996322336
Antenatal diagnosis of hereditary bullous epidermolysis. A case report

Le diagnostic antenatal des epidermolyses bulleuses hereditaires. A propos d'un cas
Aubard Y.; Genet C. // Bedane C. // Gilbert B.
Serv. de Gynecol.-Obstet. 1, CHU Dupuytren, 2, avenue Martin-Luther-King, F 87000 Limoges, France // Service de Dermatologie, CHU Dupuytren, 2, avenue Martin-Luther-King, F 87000 Limoges, France // Service de Pediatrie 1, CHU Dupuytren, 2, avenue Martin-Luther-King, F 87000 Limoges, France
Corresp. Author: Aubard Y.
Corresp. Author Affil: Service de Gynecologie-Obstetrique 1, CHU Dupuytren, 2, Avenue Martin-Luther-King, F 87000 Limoges, France

Journal de Gynecologie Obstetrique et Biologie de la Reproduction (J. GYNECOL. OBSTET. BIOL. REPROD.) (France) November 14, 1996 , 25/6 (588-593)
CODEN: JGOBA **ISSN:** 03682315
Document Type: Journal ; Article **Record Type:** Abstract
Language: French **Summary language:** French; English
Number of References: 28

A premature infant born to a consanguinous couple (mother's age = 27 years) presented Hallopeau-Siemens disease

and died at 3 weeks. At a second pregnancy, **fetal** skin **biopsies** at 21 weeks gestation demonstrated the absence of the disease. The fetus died in utero at 31 weeks of an unknown cause. A third pregnancy was **carried** to **term** successfully and terminated by delivery of a normal infant. Unlike most hereditary bullous epidermolyses, the severe prognosis of Hallopeau-Siemens disease justifies antenatal diagnosis as does Herlitz disease, another familial disease. **Fetal** skin **biopsy** at 21 weeks is classically performed, but localization of the genetic abnormalities would suggest that a simple trophoblast biopsy during the first trimester may be sufficient.

32/7/111 (Item 14 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0076231731 **EMBASE No:** 1995280284

Use of type VII collagen gene (COL7A1) markers in prenatal diagnosis of recessive dystrophic epidermolysis bullosa

Dunnill M.G.S.; Eady R.A.J. // Dunnill M.G.S.; Richards A.J.; Pope F.M. // Rodeck C.H. // Atherton D.; Lake B.D. // Petrou M.
St. John's Institute of Dermatology, St. Thomas's Hospital, Lambeth Palace Road, London SE1 7EH, United Kingdom // Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex, United Kingdom // Department of Obstetrics, Univ. College London Medical School, London, United Kingdom // Hospital for Sick Children, Great Ormond Street, London, United Kingdom // Perinatal Centre, Univ. College London Medical School, London, United Kingdom
Corresp. Author: Dunnill M.G.S.
Corresp. Author Affil: St John's Institute of Dermatology, St Thomas's Hospital, Lambeth Palace Road, London SE1 7EH, United Kingdom

Journal of Medical Genetics (J. MED. GENET.) (United Kingdom) September 1, 1995 , 32/9 (749-750)
CODEN: JMDGA **ISSN:** 00222593
Document Type: Journal ; Article **Record Type:** Abstract
Language: English **Summary language:** English
Number of References: 11

Generalised recessive dystrophic epidermolysis bullosa (EB) is a severe inherited disease in which patients suffer from blistering and scarring of the skin and mucous membranes after minor mechanical trauma. Tight genetic linkage has been established to the type VII collagen gene (COL7A1) at 3p21, with no evidence of locus heterogeneity. Several COL7A1 mutations have now been identified in recessive dystrophic EB patients. Prenatal diagnosis has been performed by examination of a **fetal** skin **biopsy** taken at about 16 weeks' gestation, and relies on identification of characteristic ultrastructural and immunohistochemical changes. We have now achieved a first trimester prenatal diagnosis using intragenic and flanking COL7A1 markers in a pregnancy at risk for recessive dystrophic EB. Segregation of the informative markers predicted the baby would be an unaffected carrier. The **pregnancy continued** to term and a healthy baby was born, confirming this result.

32/7/122 (Item 25 from file: 73) **Links**

Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0073429470 **EMBASE No:** 1987193504
Rapid prenatal diagnosis of epidermolysis bullosa letalis using GB3 monoclonal antibody

Heagerty A.H.M.; Eady R.A.J.; Kennedy A.R.; et-al
Institute of Dermatology, United Medical and Dental Schools, St. Thomas' Hospital, London SE1 7EH, United Kingdom
Corresp. Author Affil: Institute of Dermatology, United Medical and Dental Schools, St. Thomas' Hospital, London SE1 7EH, United Kingdom

British Journal of Dermatology (BR. J. DERMATOL.) (United Kingdom) October 30, 1987 , 117/3 (271-275)
CODEN: BJDEA **ISSN:** 00070963
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

The prenatal diagnosis of epidermolysis bullosa letalis was made by demonstrating a marked reduction of normal immunofluorescence staining with the monoclonal antibody GB3 in a **fetal** skin **biopsy obtained** at 18 weeks' gestation. The diagnosis was confirmed by conventional electron microscopy using established techniques. The affected **pregnancy continued** to term and a baby was delivered who rapidly developed blistering affecting the buttocks, lower limbs and mouth. This technique is simpler and quicker than electron microscopy, yet appears to retain the same degree of accuracy.

32/7/123 (Item 26 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0072913122 **EMBASE No:** 1985118538
Antenatal diagnosis of severe hereditary immunologic deficiency syndromes

DIAGNOSTIC ANTENATAL DES DEFICITS IMMUNITAIRES HEREDITAIRES GRAVES
Durandy A.; Dumez Y.; Griscelli C.
l'Unite d'Immunologie et d'Hematologie, Departement de Pediatrie et INSERM U. 132, Hopital des Enfants-Malades, 75730 Paris Cedex 15, France
Corresp. Author Affil: l'Unite d'Immunologie et d'Hematologie, Departement de Pediatrie et INSERM U. 132, Hopital des Enfants-Malades, 75730 Paris Cedex 15, France

Archives Francaises de Pediatrie (ARCH. FR. PEDIATR.) (France) July 11, 1985 , 42/3 (163-167)
CODEN: AFPEA **ISSN:** 00039764
Document Type: Journal **Record Type:** Abstract
Language: French **Summary language:** English

The recent progress in antenatal diagnosis methods led us to develop the antenatal diagnosis of several forms of hereditary and severe immune deficiencies (ID): severe combined ID (13 cases), combined ID associated with a

defective expression of HLA (2 cases), X-linked agammaglobulinemia (4 cases) and chronic granulomatous disease (1 case). Antenatal diagnosis was performed by studying by micromethods lymphocyte markers and functions in **fetal** venous blood **samples obtained** under fetoscopy (20 cases) or echography (1 case). Cytological studies were coupled with microscopical examination of the skin and the hair of a fetus at risk for Chediak-Higashi disease. These methods allowed the **continuation** of the **pregnancy** in 16 cases. Thirteen neonates were normal and two pregnancies have not yet reached term. In one case, the diagnosis of the integrity of the immune system led to the birth of a child suffering from a severe combined ID not yet described. This child was cured with a HLA semi-identical bone-marrow transplantation. An abortion was proposed for two fetuses affected with severe combined ID which was confirmed by histological examination. Two accidental abortions occurred, one of them probably as a consequence of the fetoscopy.

32/7/124 (Item 27 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0072843329 **EMBASE No:** 1985198745
Fetoscopy in the assessment of unexplained fetal hydrops

Nicolaides K.H.; Rodeck C.H.; Lange I.; et-al
Harris-Birthright Research Centre for Fetal Medicine, Department of Obstetrics and Gynaecology, Edinburgh, United Kingdom
Corresp. Author Affil: Harris-Birthright Research Centre for Fetal Medicine, Department of Obstetrics and Gynaecology, Edinburgh, United Kingdom

British Journal of Obstetrics and Gynaecology (BR. J. OBSTET. GYNAECOL.) (United Kingdom) October 23, 1985 , 92/7 (671-679)
CODEN: BJOGA **ISSN:** 03065456
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

Pure **fetal** blood **samples, obtained** fetoscopically from 30 patients with unexplained **fetal** hydrops at 16 to 32 weeks gestation were investigated for cytogenetic, haematological, biochemical and virological properties. In two patients with oligohydramnios, the fetoscope was introduced transabdominally into the fetal peritoneal cavity and sampling was undertaken from the intra-abdominal portion of the umbilical vein; in all the other patients an umbilical cord vessel was **sampled**. Ten (33%) of the **fetuses** had chromosomal abnormalities, one an erythroblastic process, possibly erythroleukaemia, one alpha-thalassaemia and one cytomegalovirus infection. Blood-film abnormalities were seen in 23 (88%) of 26 fetuses that had this examination. Biochemical analysis of fetal plasma was undertaken in 18 fetuses and hypoproteinaemia was found in all cases. One fetus was subsequently found to have a paroxysmal tachyarrhythmia that responded to digitilization. Three (10%) of the **fetuses survived**.

32/7/125 (Item 28 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0072159471 **EMBASE No:** 1982150064
Chorion biopsy in early pregnancy: A method of early prenatal diagnosis

Kazy Z.; Rozovsky I.S.; Bakharev V.A.
All-Union Res. Inst. Obstet. Gynaecol., USSR Min. Health, Moscow, U.S.S.R.
Corresp. Author Affil: All-Union Res. Inst. Obstet. Gynaecol., USSR Min. Health, Moscow, U.S.S.R.

Prenatal Diagnosis (PRENATAL DIAGN.) (United Kingdom) August 17, 1982 , 2/1 (39-45)
CODEN: PRDID **ISSN:** 01973851
Document Type: Journal **Record Type:** Abstract
Language: English

Chorion biopsy was performed in 165 cases at 6-12 weeks of pregnancy, following an ultrasonic or embryo-fetoscopic chorion frondosum localization. One hundred patients had their biopsies taken immediately before induced abortion. In 39 cases abortion was carried out 5-10 days after **biopsy**. In 26 pregnant patients **biopsy** was performed for genetic reasons. **Fetal** sex was determined in 'native' smears from **biopsy specimens** for cytological investigation, using X- and Y-chromatin assays. **Fetal** sex diagnosis proved correct in all the cases. In 40 observations, the origin of the biopsy specimen was histologically checked. In 16 biopsy specimens, a number of enzymes were simultaneously assayed: beta-D-glucosidase, beta-D-galactosidase, beta-D-hexosaminidase, beta-D-glucuronidase, alpha-L-fucosidase, beta-D-mannosidase, sphingomyelinase and arylsulphatase A. The levels of the above enzymes were compared to those observed in tissue cultures of amniotic cells obtained through amniocentesis at 16-18 weeks of pregnancy. The amniotic sac remained intact in all cases of chorion biopsy. If the **pregnancy** was **maintained** after the biopsy, no spontaneous abortions were recorded, and pregnancies resulted in the timely delivery of full-term healthy infants. Therefore, the method described is a valuable means of diagnosing inherited disorders, with promising applications in **prenatal** medicine.

32/7/129 (Item 32 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0071565700 **EMBASE No:** 1980197609
Fetoscopy and the prenatal diagnosis of inherited conditions

Rodeck C.H.
King's Coll. Hosp. Med. Sch., London SE5, Germany
Corresp. Author Affil: King's Coll. Hosp. Med. Sch., London SE5, Germany

Journal de Genetique Humaine (J. GENET. HUM.) (Switzerland) October 27, 1980 , 28/2 (41-47)
CODEN: JGHUA **ISSN:** 00217743
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

Out of a total of 202 fetoscopies, 117 were performed for diagnostic purposes in 114 patients. Three were repeated for blood **sampling** because of laboratory difficulties, although adequate **samples** of **fetal** blood had been **obtained**

at the first attempt. Interruption of pregnancy was performed in 33 and the **pregnancy continued** in 81. There were three fetal losses thought to be related to the fetoscopy. Five went into spontaneous labour between 34 and 36 weeks and 40 delivered at term; 32 patients have not yet delivered. Amniotic fluid leakage was reported in 5 pregnancies. All the babies that were delivered alive are developing normally.

32/7/130 (Item 33 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0071535921 **EMBASE No:** 1980230671
The smoking fetus: A study of the carbon monoxyde level in pregnant women and their newborns

FOETUS, FUMEUR INVOLONTAIRE; ETUDE DU MONOXYDE DE CARBONE CHEZ LES FEMMES ENCEINTES ET LES NOUVEAU
Bureau M.A.; Monette J.; Pare C.; et-al
Dept Ped., Fac. Med., Univ. Sherbrooke, Sherbrooke, Que., Canada
Corresp. Author Affil: Dept Ped., Fac. Med., Univ. Sherbrooke, Sherbrooke, Que., Canada

Union Medicale du Canada (UNION MED. CAN.) (Canada) December 15, 1980 , 109/9 (1341-1345)
CODEN: UMCAA **ISSN:** 00416959
Document Type: Journal **Record Type:** Abstract
Language: French **Summary language:** English

In this study, carried out at the Centre Hospitalier Universitaire de Sherbrooke, our objective was the measurement of the carboxyhemoglobin (HbCO) level in blood from pregnant women and their newborn. In 156 women, the HbCO level was determined on the routine **sample collected** at the first **prenatal** visit. Subsequently, the same analysis was performed on this routine blood **sample** from 241 women admitted for delivery. The analysis was then repeated at the time of delivery, and was also performed on cord blood from their newborn. There was no difference in the percentage of women who smoked at the beginning (30%) and at the end (31%) of pregnancy. Among the smokers, one in three continued to smoke during labour. The mean HbCO levels were 3.0% at first visit, 2.9% at admission and 3.0% at delivery for those who smoked during labour, but had fallen to 0.9% in the women who had stopped smoking at the start of labour. The mean HbCO was 9% in the newborns of mothers who smoked during labour. The newborn HbCO level is thus much higher than the maternal level. We conclude that current publicity against smoking does not sufficiently identify pregnant women as a high risk group when they **continue** to smoke during **pregnancy** and labour.

32/7/131 (Item 34 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0071527687 **EMBASE No:** 1980222412
Genetic amniocentesis in twin gestations

Elias S.; Gerbie A.B.; Simpson J.L.; et-al
Dept. Obstet. Gynecol., Northwest. Univ. Med. Sch., Chicago, Ill., United States
Corresp. Author Affil: Dept. Obstet. Gynecol., Northwest. Univ. Med. Sch., Chicago, Ill., United States

American Journal of Obstetrics and Gynecology (AM. J. OBSTET. GYNECOL.) (United States) December 1, 1980 , 138/2 (169-174)
CODEN: AJOGA **ISSN:** 00029378
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

Among 1,613 women studied with routine ultrasonography prior to genetic amniocentesis at Northwestern University Medical School, 25 of 26 multiple gestations were detected. Sampling of fluid from both amniotic sacs was requested by 20 women with twin gestations in which both **fetuses** were ultrasonographically determined to be **viable** and of normal size. Fluid was obtained successfully from both amniotic sacs in 19 of 20 cases. The conclusions are that twin gestations can be reliably detected by the use of routine ultrasonography, both amniotic sacs can usually be sampled, and the complication rate appears to be minimal to the patient and the **fetuses**, although the **sample** size is still small.

32/7/132 (Item 35 from file: 73) **Links**
Fulltext available through: STIC Full Text Retrieval Options
EMBASE

0071490237 **EMBASE No:** 1979223227
Prenatal evaluation of fetus at risk for severe von Willebrand's disease

Hoyer L.W.; Lindsten J.; Blomback M.; et-al
Dept. Blood Coagul. Res., Karolinska Inst., S-104 01 Stockholm, Sweden
Corresp. Author Affil: Dept. Blood Coagul. Res., Karolinska Inst., S-104 01 Stockholm, Sweden

Lancet (LANCET) (United Kingdom) November 15, 1979 , 2/8135 (191-192)
CODEN: LANCA **ISSN:** 01406736
Document Type: Journal ; Letter **Record Type:** Abstract
Language: English

While most patients with von Willebrand's disease (vWD) are heterozygous and have only a mild bleeding problem, an individual who is homozygous for the vWD allele(s) has very low levels of factor VIII and may have a severe haemorrhagic disorder. If both parents have heterozygous vWD their children may have the severe form of this condition. The development of sensitive immunoradiometric assays for components of the factor VIII complex and improvement in techniques for **obtaining fetal** blood have made **prenatal** diagnosis possible for fetuses at risk for haemophilia. We report here the prenatal evaluation of factor VIII in a fetus at risk for severe vWD. The values for factor VIIR:Ag were normal. Although the prenatal assessment in respect of vWD was evident from the VIIIR:Ag measurements, we also determined VIII:C(Ag). The values were normal in two **samples**; the third was too dilute for VIII:C(Ag) measurement. Although mild (heterozygous) vWD could not be ruled out, these data excluded the severe form. **Pregnancy continued** to term without complications. Labour started spontaneously in the 38th week, and a boy was delivered by caesarean section because of breech presentation and a borderline pelvis.

Coagulation studies, including VIII:Ag, were normal and the infant had no abnormal bleeding. Unfortunately, the child had a complex of skeletal malformations including bilateral femoral hypoplasia and club foot, cleft palate, and micrognathia. This is a recognized pattern of malformations. Chromosome studies were normal.

32/7/133 (Item 36 from file: 73) **Links**
EMBASE

0070718749 **EMBASE No:** 1977075564
Prenatal diagnosis of hemoglobinopathies INTRAUTERINE FETAL VISUALIZATION: A MULTIDISCIPLINARY APPROACH

Klein P.H.; Wai Kan Y.
Univ. California, Sch. Med., San Francisco, Calif. 94122, United States
Corresp. Author Affil: Univ. California, Sch. Med., San Francisco, Calif. 94122, United States

EXCERPTA MED., AMSTERDAM, I.C.S. December 1, 1976 , no.371/- (132-135)
CODEN: BOOKA
Document Type: Book **Record Type:** Abstract
Language: English

Biochemical techniques necessary for **prenatal** diagnosis of sickle cell disease, and alpha and probably beta thalassemia are now available. It may now be possible to diagnose sickle cell anemia in placental blood containing as little as 1% fetal cells. More investigation is needed, however, to determine if beta thalassemia can be diagnosed in the fetus. Rapid advances have been made in the techniques of obtaining placental blood; however, the methods of sampling must still be perfected and subsequently evaluated for their effects on the fetus and the course of pregnancy. Once these technical problems are solved, **prenatal** diagnosis can be a clinical reality. Recently, the techniques outlined above have been successfully applied to **prenatal** diagnosis of beta thalassemia. A couple of Sicilian extraction have a 5 year old girl with homozygous beta SUP + thalassemia severe enough to require monthly transfusion therapy. The mother was again pregnant and they did not wish to **continue** with the **pregnancy** unless they could have some indication that the fetus would not be affected by beta thalassemia. At 20 weeks' gestation, **prenatal** diagnosis was attempted and a **sample** of pure **fetal** blood was **obtained**. Studies showed that the level of beta chain synthesized by the **fetal** blood was in the low normal range. Thus, the child is probably normal and at most heterozygous for beta thalassemia. On this basis, the parents decided to continue with the pregnacy. This represents the first time **prenatal** diagnosis has been used in a pregnancy at risk for thalassemia or a hemoglobinopathy. It demonstrates the positive aspect of **prenatal** diagnosis. Reassurance of these parents has allowed this pregnancy, which might otherwise have been terminated, to continue. Frequently, parents of a child with homozygous beta thalassemia will not have any more children. If the techniques described herein prove to be persistently successful, these parents will be able to have healthy children.

32/7/135 (Item 38 from file: 73) **Links**
EMBASE

0070295549 **EMBASE No:** 1975079335

Cyclohexylamine mutagenicity: An in vivo evaluation utilizing fetal lambs

Turner J.H.; Hutchinson D.L.
Grad. Sch. Publ. Hlth., Univ. Pittsburgh, Pa. 15261, United States
Corresp. Author Affil: Grad. Sch. Publ. Hlth., Univ. Pittsburgh, Pa. 15261, United States

Mutation Research (MUTAT. RES.) December 1, 1974 , 26/5 (407-412)
CODEN: MUREA
Document Type: Journal ; Article **Record Type:** Abstract
Language: English

The **in vivo** effects of cyclohexylamine (CHA) upon the segregation apparatus and chromosome morphology of mitogenically capable lymphocytes **obtained** from the peripheral circulating blood **tissue** of **living fetal** lambs **in utero** were evaluated. CHA proved to be a clastogen **in vivo**. The mechanism(s) of chromosome effect was evidently expressed during both G SUB 1 and S G SUB 2 phases of the cellular autosynthetic cycle. Increases in numerical aberrations were not observed but the chemical was found to produce **in vivo** toxicity in that a dose related inhibition of growth was an observable concomitant of increasing levels of treatment.

32/7/148 (Item 12 from file: 5) **Links**
Fulltext available through: STIC Full Text Retrieval Options
Biosis Previews(R)

07201781 **Biosis No.:** 198477033692
PRE NATAL DIAGNOSIS OF SICKLE CELL ANEMIA IN THE 1ST TRIMESTER OF PREGNANCY

Author: GOOSSENS M (Reprint); DUMEZ Y; KAPLAN L; LUPKER M; CHABRET C; HENRION R; ROSA J
Author Address: SERVICE BIOCHEMIE, INSERM U 91, HOPITAL HENRI MONDOR, 94010 CRETEIL, FR** FRANCE
Journal: New England Journal of Medicine 309 (14): p 831-833 1983
ISSN: 0028-4793
Document Type: Article
Record Type: Abstract
Language: ENGLISH

Abstract: To investigate the usefulness of chorionic **biopsy** for **prenatal** diagnosis of sickle-cell anemia by restriction-endonuclease analysis of fetal DNA, 30 pregnancies were studied before elective abortion. When the reproducibility of the technique for **obtaining** adequate DNA **samples** was established, the test was successfully applied to 5 pregnancies at risk for sickle-cell anemia. In 2 cases sickle-cell disease of the fetus led to a decision to terminate the pregnancy. In 3 other cases a normal or AS genotype was demonstrated. One normal infant has been born and 1 other **pregnancy** is **continuing** normally. In one case in which fetal death was observed 3 wk after sampling, placental abnormalities found on histologic examination were compatible with a chromosomal aberration. Chorionic **biopsy** is feasible for the **prenatal** diagnosis of [human] sickle-cell disease before the 10th gestational wk. If subsequent experience demonstrates this technique to be safe enough for mother and fetus, the ability to test in early pregnancy may make prenatal diagnosis acceptable to more couples at risk for serious genetic disorders.

32/7/149 (Item 13 from file: 5) **Links**
Fulltext available through: STIC Full Text Retrieval Options
Biosis Previews(R)

06622890 **Biosis No.:** 198274039313
CHORION BIOPSY IN EARLY PREGNANCY A METHOD OF EARLY PRE NATAL DIAGNOSIS FOR INHERITED DISORDERS

Author: KAZY Z (Reprint); ROZOVSKY I S; BAKHAREV V A
Author Address: ALL-UNION RESEARCH INST OF OBSTETRICS AND GYNAECOL, USSR MINISTRY OF HEALTH **USSR
Journal: Prenatal Diagnosis 2 (1): p 39-46 1982
ISSN: 0197-3851
Document Type: Article
Record Type: Abstract
Language: ENGLISH

Abstract: Chorion biopsy was performed in 165 cases at 6-12 wk of pregnancy, following an ultrasonic or embryo-fetoscopic chorion frondosum localization. Patients (100) had their biopsies taken immediately before induced abortion. In 39 cases abortion was carried out 5-10 days after **biopsy**. In 26 pregnant patients **biopsy** was performed for genetic reasons. **Fetal** sex was determined in native smears from **biopsy specimens** for cytological investigation, using X- and Y-chromatin assays. **Fetal** sex diagnosis proved correct in all the cases. In 40 observations, the origin of the biopsy specimen was histologically checked. In 16 biopsy specimens, a number of enzymes were simultaneously assayed: .beta.-D-glucosidase, .beta.-D-galactosidase, .beta.-D-hexosaminidase, .beta.-D-glucuronidase, .alpha.-L-fucosidase, .beta.-D-mannosidase, sphingomyelinase and arylsulfatase A. The levels of the above enzymes were compared to those observed in tissue cultures of amniotic cells obtained through amniocentesis at 16-18 wk of pregnancy. The amniotic sac remained intact in all cases of chorion biopsy. If the **pregnancy** was **maintained** after the biopsy, no spontaneous abortions were recorded, and pregnancies resulted in the timely delivery of full-term healthy infants. The method described is a valuable means of diagnosing inherited disorders, with promising applications in **prenatal** medicine.

32/7/150 (Item 14 from file: 5) **Links**
Fulltext available through: STIC Full Text Retrieval Options
Biosis Previews(R)

05977733 **Biosis No.:** 198070009220
IN UTERO PATERNITY TESTING UTILIZING FETAL BLOOD OBTAINED BY MID TRIMESTER FETOSCOPY

Author: GOLBUS M S (Reprint); STEPHENS J D; CANN H M
Author Address: DEP OBSTET GYNECOL, UNIV CALIF, SAN FRANCISCO, CALIF 94143, USA**USA
Journal: American Journal of Human Genetics 32 (1): p 88-91 1980
ISSN: 0002-9297

Document Type: Article
Record Type: Abstract
Language: ENGLISH

Abstract: To evaluate paternity in a case where rape and conjugal coitus had occurred close to the time of conception, fetoscopy with **fetal** blood **sampling** was performed at 20 wk gestation. Detailed blood group typing of the wife, husband and fetus, and the presence of a very long Y chromosome in the last 2, indicated a 99.9% chance that the fetus was fathered by the husband and only a 0.1% chance that the fetus was fathered by some other male Caucasian. The couple elected to **continue** the **pregnancy**. Neonatal testing verified the prenatal findings.

32/7/165 (Item 2 from file: 144) Links
Fulltext available through: STIC Full Text Retrieval Options
Pascal

15807999 PASCAL No.: 02-0524419

Fetal tissue engineering: **In utero** tracheal augmentation in an ovine model. Discussion
2001 Annual Meeting of the Section on Surgery of the American Academy of Pediatrics, San Francisco, California, October 19-21, 2001

FUCHS Julie R; TERADA Shinichi; OCHOA Erin R; VACANTI Joseph P ; FAUZA Dario O; GITTES G comment
KANDEL Jessica, ed
Harvard Center for Minimally Invasive Surgery, Harvard Medical School, Center for the Integration of Medicine and Innovative Technologies, Massachusetts General Hospital, and Children's Hospital, Boston, MA, United States
Babies Hospital, Columbia University, New York, New York, United States
American Academy of Pediatrics. Section on Surgery, United States
Annual Meeting of the Section on Surgery of the American Academy of Pediatrics (San Francisco, California USA) 2001-10-19
Journal: Journal of pediatric surgery, 2002, 37 (7) 1000-1006
ISSN: 0022-3468 CODEN: JPDSA3 Availability: INIST-14715 ; 354000108892370120
No. of Refs.: 25 ref.
Document Type: P (Serial); C (Conference Proceedings) ; A (Analytic)
Country of Publication: United States
Language: English
Background/Purpose: This study was aimed at comparing fetal tissue engineering with autologous free grafting in an ovine model of **in utero** tracheal repair. Methods: Chondrocytes were isolated from both elastic and hyaline cartilage **specimens harvested** from **fetal** lambs and expanded in vitro. Cells were seeded dynamically onto biodegradable scaffolds, which then were maintained in a rotating

bioreactor for 6 to 8 weeks. Constructs subsequently were implanted into fetal tracheas (n = 15), in a heterologous fashion (group I). In group II, fetuses (n = 5) received autologous free grafts of elastic cartilage harvested from the ear as tracheal implants. **In vivo** specimens were harvested for histologic analysis at different time-points postimplantation. Results: In the 12 of 15 **surviving fetuses** of group I, all constructs were found to resemble normal hyaline cartilage, engraft well despite their heterologous origin, and display time-dependent epithelialization derived from the native trachea. All autologous free grafts were engrafted and epithelialized at birth, retaining histologic characteristics of elastic cartilage, but were more deformed than engineered constructs. Of the lambs allowed to reach term, 5 of 5 in the engineered group and 4 of 5 in the free graft group could breathe spontaneously. Conclusions: (1) Tissue-engineered cartilage, as well as autologous free grafts, can be implanted successfully into the fetal trachea, resulting in engraftment and function. (2) Engineered cartilage provides enhanced structural support after implantation into the fetal trachea when compared with free grafts. **Prenatal** tracheoplasty may prove useful for the treatment of severe congenital tracheal malformations.

32/7/171 (Item 1 from file: 35) **Links**
Dissertation Abs Online

02228380 ORDER NO: AADAA-IC828772

Characterisation of human foetal femur-derived cells and their potential for bone tissue regeneration

Author: Mirmalek-Sani, Sayed-Hadi
Degree: Ph.D.
Year: 2006
Corporate Source/Institution: University of Southampton (United Kingdom) (5036)
Source: Volume 6803C of Dissertations Abstracts International.
PAGE 693

With an increasingly aging population, the requirement of skeletal tissue repair is a major socio-economic need. An emergent approach, skeletal tissue engineering, promises new strategies to combat skeletal injury and repair through stem cell-based tissue regeneration. To date, the plasticity, multipotentiality and characteristics of potential stem cells from early foetal skeletal tissue remain poorly defined. Our aim was to characterise human foetal femur-derived cells in comparison to adult-derived mesenchymal populations.

Cells were expanded in basal conditions from explant cultures of human foetal femurs at 8–12 weeks post conception. Foetal-derived cells expressed type I collagen, stromal antigens STRO-1, CD63, CD166, germ cell marker TRA-1-60 and were negative for embryonic markers NANOG, SSEA-3 and OCT-4. Expression of STRO-1 in **foetal samples** ranged from 2.8–10.2% and was seen in basal conditions after 21 days and as late as passage 3. Cell proliferation studies indicated a doubling time of 21.5±1.0 hrs. Multilineage differentiation potential of individual foetal femur-derived cells was demonstrated in clonal studies. Expression of

peroxisome-proliferator activated receptor-γ (PPAR-γ) and aP2 (fatty acid binding protein-3) was observed in adipogenic conditions and osteogenic differentiation was confirmed by expression of alkaline phosphatase, osteopontin and osteocalcin. In chondrogenic conditions, cells were embedded within lacunae and extensive matrix deposition was observed. Differentiation and proliferation were accelerated in foetal populations compared to adult-derived cells, however loss of expansion potential and marked morphological change within foetal populations was observed after serial passages. Expansion of foetal cells in a serum-free chemically defined medium suggests effective future <italic>ex vivo</italic> expansion strategies for cell-based tissue regeneration. Growth on a variety of biomimetic scaffolds was demonstrated, with differentiation to the osteogenic lineage and maintained cell viability <italic> in vitro</italic>. Utilising the immunodeficient mouse model, <italic>**in vivo** </italic> studies demonstrated **survival** and expansion of **foetal**-derived cells and integration within a critical size bone defect.

Although questions remain over the immunogenicity and practical use of foetal-derived cells, these studies demonstrate their use as a unique alternate cell source to examine mesenchymal stem cell biology in the development of strategies for the restoration of damaged or diseased tissue.

?

A service of the U.S. National Library of Medicine
and the National Institutes of Health

My NCBI [?]
[Sign In] [Register]

Advanced Search

harvest* fetal tissue* | Preview | Search

PubMed Search History

- Search History will be lost after eight hours of inactivity.
- Search numbers may not be continuous; all searches are represented.
- To save search indefinitely, click query # and select Save in My NCBI.
- To combine searches use #search, e.g., #2 AND #3 or click query # for more options.

Search	Most Recent Queries	Time	Results
#8	**Search harvest* fetal tissue***	**17:09:11**	**99**
#7	Search **harvest* fetus tissue* (suction* OR pressure)**	16:43:15	0
#6	Search **harvest* fetal tissue* (suction* OR pressure)**	16:42:54	1
#5	Search **harvest* fetal tissue***	16:42:39	99
#1	Search **Bonutti P[author]**	16:28:34	34

More History | Clear History

Search by Author, Journal, Publication Date, and more

Fill in any or all of the fields below, as needed.

◉ All of these (AND) ○ Any of these (OR)

Search Author for

Search Journal for

Search Publication Date for to present
(yyyy/mm/dd - month and day are optional)

Add More Search Fields

Clear All Search

Limit by Topics, Languages, and Journal Groups

Full Text, Free Full Text, and Abstracts CLEAR

☐ Links to full text ☐ Links to free full text ☐ Abstracts

Humans or Animals CLEAR
- ☐ Humans
- ☐ Animals

Gender CLEAR
- ☐ Male
- ☐ Female

Type of Article CLEAR
- ☐ Clinical Trial
- ☐ Editorial
- ☐ Letter
- ☐ Meta-Analysis
- ☐ Practice Guideline

Languages CLEAR
- ☐ English
- ☐ French
- ☐ German
- ☐ Italian
- ☐ Japanese

Subsets CLEAR

Journal Groups
- ☐ Core clinical journals
- ☐ Dental journals
- ☐ Nursing journals

Topics

Ages CLEAR
- ☐ All Infant: birth-23 months
- ☐ All Child: 0-18 years
- ☐ All Adult: 19+ years
- ☐ Newborn: birth-1 month
- ☐ Infant: 1-23 months

Clear All Search

Index of Fields and Field Values

Add Term(s) to the search box or view an index.

All Fields | Preview | Index

Add to Search Box with: AND | OR | NOT

KARGER

Fetal Diagnosis and Therapy

Vol. 15, No. 2, 2000

Paper

Molecular and Fetal Tissue Biopsy Capabilities Are Needed to Maximize Prenatal Diagnosis of Junctional Epidermolysis bullosa: Fetal Skin Biopsy Using a 1-mm Microendoscope

David E. Seubert, Baruch Feldman, Eric L. Krivchenia, Mark I. Evans, Gerard Barki, Richard Leach, Mark P. Johnson

Center for Fetal Diagnosis, Department of Obstetrics and Gynecology, Molecular Medicine and Genetics and Pathology, Wayne State University/Hutzel Hospital, Detroit, Mich., USA

Address of Corresponding Author

Fetal Diagn Ther 2000;15:89-92 (DOI: 10.1159/000020982)

Key Words

- Fetoscopy
- In-utero biopsy

Abstract

Objective: To describe a minimally invasive micro-endoscopic technique for fetal skin biopsy and direct examination for a lethal skin condition. *Materials and Methods:* Direct fetoscopic examination of a fetus was undertaken along with full thickness skin biopsies at 19 weeks' gestation. *Results:* No phenotypic expressions of the lethal condition were visualized and six full thickness skin biopsies were collected. Pathological examination revealed normal skin structures not consistent with junctional epidermolysis bullosa (JEB). *Conclusion:* Minimally invasive examination with the 1 mm endoscope allows direct fetal phenotypic evaluation, full thickness skin biopsies, with risks similar to amniocentesis.

Author Contacts

David E. Seubert, MD
Department of Obstetrics and Gynecology
Wayne State University/Hutzel Hospital
4707 St. Antoine Blvd., Detroit, MI 48201 (USA)
Tel. +1 313 745 7583, Fax +1 313 993 2685, E-Mail dseubert@med.wayne.edu

---

Article Information

Received: Received: August 10, 1999
Accepted: October 18, 1999
Number of Print Pages : **4**
Number of Figures : **4**, Number of Tables : **0**, Number of References : **11**

```
Set     Items   Description
S1      33466   S FETUS?? OR FOETUS?? OR FAETUS?? OR FETAL? OR FOETAL? OR FAETAL? OR
EMBRYO? ? OR EMBRYONIC? OR UNBORN? OR (UN OR "NOT" OR PRIOR OR BEFORE)(2W)(BORN??? OR
BIRTH???) OR (PRE()TERM? ? OR PRETERM?)(5N) (BABY? ? OR BABIES OR CHILD? ? OR CHILDREN? OR
OFFSPRING? OR OFF()SPRING? ?)
S2       4403   S IN()(UTERO OR VIVO OR VENTER) OR PRE()NATAL??? OR PRENATAL? OR (INSIDE
OR IN OR WITHIN)(3N)(UTERUS? OR WOMB? ? OR UTERI? ?)
S3       3710   S VIABLE? OR VIABILIT? OR ALIVE OR LIVE OR LIVES OR LIVED OR LIVING OR
SURVIV?
S4         58   S (MAINTAIN? OR SUSTAIN? OR CONTINU?)(3N)(PREGNANCY OR PREGNANT) OR
(CARRY? OR CARRIE? ?)(2N)(TERM? ? OR FULLTERM?)
S5      19938   S HARVEST? OR BIOPSY? OR BIOPSIE? ? OR SAMPLING? OR SAMPLE? ? OR REMOV? OR
EXTRACT? OR RESECT? OR WITHDRAW? OR COLLECT? OR EXCIS??? OR EXCISION? OR OBTAIN??? OR
(TAKE? ? OR TAKING OR TOOK)()OUT
S6       4067   S S1 (5N) S5
S7       7254   S S5 (5N) (TISSUE? ? OR BONE OR MASS OR SPECIMEN? OR SAMPLE? ?)
S8        595   S S1(5N)S3
S9        242   S S2(5N)S5
S10        10   S S6:S7 AND (S4 OR S8) AND S9
S11      1567   S S5(5N)S1(5N)(TISSUE? ? OR BONE OR MASS OR SPECIMEN? OR SAMPLE? ?)
S12        25   S S11 AND (S4 OR S8) AND S2
S13        19   S S12 NOT S10
S14        38   S S11 (S) (S4 OR S8)
S15        26   S S14 NOT (S10 OR S13)

?  show files
```

[File 350] **Derwent WPIX** 1963-2008/UD=200831

[File 347] **JAPIO** Dec 1976-2007/Dec(Updated 080328)

```
Set     Items   Description
S1        519   S AU=(BONUTTI P? OR BONUTTI, P?)
S2         11   S S1 AND (FETUS?? OR FOETUS?? OR FETAL? OR FOETAL? OR EMBRYO? ? OR
EMBRYONIC? OR UNBORN? OR (UN OR "NOT" OR PRIOR OR BEFORE)(2W)(BORN??? OR BIRTH???))
S3         11   S S2 FROM 350, 347
 ; show files
```

[File 350] **Derwent WPIX** 1963-2008/UD=200831
(c) 2008 The Thomson Corporation. All rights reserved.

[File 347] **JAPIO** Dec 1976-2007/Dec(Updated 080328)
(c) 2008 JPO & JAPIO. All rights reserved.

[File 155] **MEDLINE(R)** 1950-2008/May 14
(c) format only 2008 Dialog. All rights reserved.
**File 155: MEDLINE has reloaded. Please see HELP NEWS 155 for details.*

[File 73] **EMBASE** 1974-2008/May 15
(c) 2008 Elsevier B.V. All rights reserved.
**File 73: The 2008 EMTREE Thesaurus has been loaded. Please see HELP NEWS 72 for details.*

[File 5] **Biosis Previews(R)** 1926-2008/May W2
(c) 2008 The Thomson Corporation. All rights reserved.

[File 35] **Dissertation Abs Online** 1861-2008/Nov
(c) 2008 ProQuest Info&Learning. All rights reserved.

[File 65] **Inside Conferences** 1993-2008/May 16
(c) 2008 BLDSC all rts. reserv. All rights reserved.

1: Am J Obstet Gynecol. 1985 Nov 15;153(6):655-60.

Fetal blood sampling during pregnancy with use of a needle guided by ultrasound: a study of 606 consecutive cases.

Daffos F, Capella-Pavlovsky M, Forestier F.

Because of various prenatal diagnoses, 606 fetal blood samplings were carried out in 562 pregnancies from the gestational week 17 to 38 with use of a 20-gauge needle guided by ultrasound. The procedure was performed on outpatients under local anesthesia and without medication before or after the procedure. Pure fetal blood was obtained at the first attempt in 588 cases. A second attempt was necessary in 18 cases. Maternal blood contamination was never present. Amniotic fluid dilution was noted in 15 cases. At the beginning of our experience only three cords could not be punctured. The duration of the procedure was less than 10 minutes in 90% of cases. Fifty-eight pregnancies were terminated after consideration of the results of the diagnosis, and 504 pregnancies were continued. The complications found in these pregnancies were premature delivery (5%), growth retardation (8%), in utero death (1.1%), and spontaneous abortion (0.8%). In the future this new procedure could replace fetoscopy and initiate an important field of new investigations.

PMID: 3904460 [PubMed - indexed for MEDLINE]

3/25/1 (Item 1 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0017165890 & & *Drawing available*
WPI Acc no: 2007-880843/200781
XRAM Acc no: C2007-300439
XRPX Acc No: N2007-699554
Medical system for administration of pharmaceutical agent in vivo to patient, transmits energy signal to layers of reactive coating in medical implant for increasing release rate of pharmaceutical agent between layers
Patent Assignee: BONUTTI P M (BONU-I); CREMENS M J (CREM-I)
Inventor: **BONUTTI P M**; CREMENS M J

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20070141106	A1	20070621	200781	B

US 20070141106
Local Applications (no., kind, date): US 2005728206 P 20051019; US 2006549994 A 20061017
Priority Applications (no., kind, date): US 2005728206 P 20051019; US 2006549994 A 20061017

Alerting Abstract US A1
NOVELTY - A biodegradable medical implant (10) positioned in body of patient, including pharmaceutical agent (12) interposed between layers of biodegradable reactive coating used for control the release of pharmaceutical agent. An energy unit (32) transmits an energy signal (33) to the layers of reactive coating for increasing the release rate of pharmaceutical agent.
DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

1. method of releasing pharmaceutical agent from medical implant; and
2. medical implant for administration of pharmaceutical agent.

USE - For administrating pharmaceutical agent such as heparin, heparin fragments, colchicine, taxol, agiotensin converting enzyme (ACE) inhibitor, angiopeptin, cyclosporin A, goat-anti-rabbit platelet derived growth factor (PDGF) antibody, terbinafine, trapidil, interferon-gamma, steroids, ionizing radiation, fusion toxin, antisense oligonuleotides, gene vectors and rapamycin used for treating restenosis. And also for administrating pharmaceutical agent such as hormones, cells, **fetal** cells, stem cells, bone morphogenic protein (BMP), tissue inductive factor, enzyme, protein, RNA, viruses, etc., in vivo to patient using medical implant such as stent.
ADVANTAGE - The release rate of the pharmaceutical agent into the body of patient is controlled effectively by using energy unit.
DESCRIPTION OF DRAWINGS - The figure shows a perspective view of the energy unit in use with medical implant.
10 Medical implant
12 Pharmaceutical agent

32 Energy unit
33 Energy signal

3/25/2 (Item 2 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0015753740 & *& Drawing available*
WPI Acc no: 2006-315519/200633
XRAM Acc no: C2006-103716
XRPX Acc No: N2006-268288
Intervertebral disc surgery method for, e.g. repairing tissue, by creating passage in vertebral body adjacent to the disc, in which the passage extends from side surface of the vertebral body to nucleus pulposus of the disc
Patent Assignee: BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20060089646	A1	20060427	200633	B

US 20060089646
Local Applications (no., kind, date): US 2004622095 P 20041026; US 2005258795 A 20051026
Priority Applications (no., kind, date): US 2004622095 P 20041026; US 2005258795 A 20051026

Alerting Abstract US A1
NOVELTY - Intervertebral disc surgery method involves creating a passage in a vertebral body adjacent to the intervertebral disc. The passage extends from a side surface of the vertebral body to a nucleus pulposus of the intervertebral disc.
USE - The method is used for performing intervertebral disc surgery. It is used for repairing and stabilizing tissue and implants; repairing, reconstructing, augmenting, and stabilizing joints of the body, the knee and joints of the spine (including intervertebral discs and adjacent bones).
ADVANTAGE - The inventive method for the repair, reconstruction, augmentation, and securing of tissue or implants during a surgical procedure and on the way out after the surgical procedure has been performed. Hard and soft tissue at and around the operation site and tissue between the operation site and the skin incision may be compressed and/or rebuilt so that tissue-function is partially restored and the operation region is stabilized for enhanced healing.
DESCRIPTION OF DRAWINGS - The figure illustrates a total intervertebral disc replacement implant.
82, 84 Vertebrae
106, 108 Spinous processes
110 Implant

3/25/3 (Item 3 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0015551303
WPI Acc no: 2006-115457/200612
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293

; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRAM Acc no: C2006-040913
XRPX Acc No: N2006-099893
Processing cells implantable in a recipient for therapy, comprises harvesting tissue fragments from a donor, separating cells from the fragments, and placing the cells in a form until implantation
Patent Assignee: BONUTTI IP LLC (BONU-N)
Inventor: **BONUTTI P M**

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 6990982	B1	20060131	200612	B

US 6990982
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 200244388 A 20020111; US 2003386856 A 20030312
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US

2000483676 A 20000114; US 200244388 A 20020111; US 2003386856 A 20030312

Alerting Abstract US B1
NOVELTY - Processing cells implantable in a recipient for therapeutic use, comprises:

A. harvesting tissue fragments from several locations within a tissue of a donor from one percutaneous incision;
B. separating cells from the tissue fragments; and
C. placing the cells in a form until implantation, where the tissue fragments contain cartilage tissue and the cells are viable.

DESCRIPTION - Processing cells implantable in recipient for therapeutic use, comprises:

A. harvesting tissue fragments from several locations within a tissue of a donor from one percutaneous incision, separating cells from the tissue fragments, and placing the cells in a form until implantation, where the tissue fragments contain cartilage tissue and the cells are viable; or
B. harvesting tissue fragments from several locations within a tissue of a donor from one percutaneous incision, separating cells from the tissue fragments, and combining the cells with a material chose from tissue grafts, collagen, antibiotics and bone growth promoting substances, where the cells are viable and tissue fragments contain tissue chosen from bone, cartilage, muscle and **fetal** tissue.

USE - For processing cells implantable in a recipient for therapeutic use (claimed).
ADVANTAGE - (M1) Is efficient.

3/25/4 (Item 4 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0013329327 *& & Drawing available*
WPI Acc no: 2003-416704/200339
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701;

2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2003-332167

Percutaneous tissue removal and implantation method involves combining harvested tissue elements with collagen and forming grafting material to implant in patient

Patent Assignee: BONUTTI 2003 TRUST-A (BONU-N); BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (2 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20030009237	A1	20030109	200339	B
US 6719803	B2	20040413	200425	E

US 20030009237
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233865 A 20020903 ; US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233865 A 20020903
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233865 A 20020903

Alerting Abstract US A1

NOVELTY - The tissue elements are harvested from a donor and combined with substance such as collagen, tissue grafts and antibiotics, to form a grafting material. The grafting material is then implanted in a patient.
USE - For removal and implantation of bone tissue, cartilage, muscle, **fetal** tissue.
ADVANTAGE - Supports bone in growth as the tissue elements are combined with substances such as grafts, collagen, antibiotics. Provides safe and efficient way to collect and reuse patient's bone without damaging the skin, muscle and bones and without causing much pain, as there is only intraosseous bleeding.
DESCRIPTION OF DRAWINGS - The figure shows the schematic view of harvested tissue fragments into compressed plug.

3/25/5 (Item 5 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0013164805 *& & Drawing available*
WPI Acc no: 2003-247723/200324
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2003-196930
Surgical instrument positioning system has several inflatable elements provided in tip positioning unit which is located at end of flexible drill shaft
Patent Assignee: BONUTTI 2003 TRUST-A (BONU-N); BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (2 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20030009172	A1	20030109	200324	B
US 6592531	B2	20030715	200348	E

US 20030009172
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233889 A 20020903 ; US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233889 A 20020903
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233889 A 20020903

Alerting Abstract US A1
NOVELTY - A tip positioning unit (160) located at the distal end of a flexible drill shaft (152), comprises several inflatable elements (162).
USE - For cutting and removing selected portions of tissue from patient e.g. bone tissue, cartilage, muscle, **fetal** tissue, removal of kidney stones, gall bladder stones, tumor, etc.

ADVANTAGE - Selective removal of tissue is performed reliably and easily. Safety operations for collecting tissue and reusing it is attained.
DESCRIPTION OF DRAWINGS - The figure shows a schematic view of the surgical instrument positioning system.
152 drill shaft
160 tip positioning unit
162 inflatable elements

3/25/6 (Item 6 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0013138570 & & *Drawing available*
WPI Acc no: 2003-220849/200321
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2003-176250
Percutaneous tissue removal method e.g. for bone tissue, involves introducing biodegradable sac into space created by inflating inflatable mechanism inserted into tissue through flexible drill shaft
Patent Assignee: BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20030009147	A1	20030109	200321	B

US 20030009147

Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233866 A 20020903
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002233866 A 20020903

Alerting Abstract US A1
NOVELTY - An inflatable mechanism is inserted into a percutaneous tissue and is inflated, to create a space in the tissue. A biodegradable sac selected from the group consisting of tissue grafts, collagen, antibiotics, or bone growth promoting substances, is introduced into the space through a flexible drill shaft (14). A cutting tip (16) is mounted on the shaft, for cutting the tissue. The process is performed under x-ray guidance.
USE - For removing percutaneous tissue e.g. bone tissue, cartilage, muscle, **fetal** tissue, etc. Also for removal of stones in kidney gall bladder, stone or tumor in stomach, polyp or tumor in colon, etc., and for tissue grafting for surgical applications.
ADVANTAGE - Since the drill shaft is flexible, the surgeon guides the cutting tip fixed to the shaft, to various locations within the tissue from one percutaneous incision and the surgeon cuts around arcs or angles, to reach any desired location, and to avoid vital tissue which would otherwise be in the cutting path.
DESCRIPTION OF DRAWINGS - The figure shows the block diagram of the percutaneous tissue removal system.
14 flexible drill shaft
16 cutting tip

3/25/7 (Item 7 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0012847532 *& & Drawing available*
WPI Acc no: 2002-706046/200276
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704;

2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2002-556627

Percutaneous tissue removal apparatus has motor that provides rotational movement to drill shaft for moving cutting tip against tissue to cut tissue fragments from tissue

Patent Assignee: BONUTTI P M (BONU-I); BONUTTI IP LLC (BONU-N)
Inventor: **BONUTTI P M**

Patent Family (2 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20020099401	A1	20020725	200276	B
US 7134437	B2	20061114	200677	E

US 20020099401
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002104250 A 20020322 ; US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002104250 A 20020322
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2002104250 A 20020322

Alerting Abstract US A1
NOVELTY - A motor (20) provides rotational motion to a flexible drill shaft (14) for moving cutting tip (16) against a tissue to cut tissue fragments from the tissue. A guide rod removes the tissue fragments along the shaft by suction to a desired location outside the body while cutting the tissue.
DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

C. Human tissue removal method; and
D. Human tissue grafting method.

USE - For removal of tissue, cartilage, muscle **fetal** tissue, kidney, gall bladder stone, tumor or polyp in colon for medical surgery such as endoscopic, arthroscopic, fiber optic, open surgery for implantation.
ADVANTAGE - Surgeon can cut around arcs or angles rather than being able to go in a straight line to reach any desired location and remove tissue without any injury to adjacent surfaces, since the drill shaft can deform while removing the tissue.
DESCRIPTION OF DRAWINGS - The figure shows the schematic view of the tissue removal apparatus.
14 Drill shaft
16 Cutting tip
20 Motor

3/25/8 (Item 8 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0012816138 & & *Drawing available*
WPI Acc no: 2002-673585/200272
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRAM Acc no: C2002-189741
XRPX Acc No: N2002-532529
Harvesting cells for therapeutic use, by cutting tissue fragments from donor tissue, collecting or suctioning the tissues outside the donor, separating cells from the tissues and implanting viable cells into a recipient
Patent Assignee: BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (2 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20020091403	A1	20020711	200272	B
US 6543455	B2	20030408	200327	E

US 20020091403
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 200244388 A 20020111; US 200244388 A 20020111
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 200244388 A 20020111

Alerting Abstract US A1
NOVELTY - Harvesting (M) cells for therapeutic use, by cutting tissue fragments (TF) from a donor tissue, collecting TF or suctioning TF through a shaft (14) at a location outside the donor, separating cells from TF and implanting the cells into a recipient, where the cells are viable, is new.
USE - (M) is useful for harvesting cells for therapeutic use, where the donor and recipient are the same or different individuals (claimed).
ADVANTAGE - (M) does not create any stress risers which would weaken the bone. (M) provides a safe and efficient way to collect and reuse a patient's own tissue.
DESCRIPTION OF DRAWINGS - The figure shows a schematic view of a tissue removal system including a flexible drill.
14 Shaft

3/25/9 (Item 9 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0012780820 & *& Drawing available*
WPI Acc no: 2002-635503/200268
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2002-502030
Tissue removal apparatus has cutting tip mounted on flexible drill shaft for cutting tissue fragments which are removed along shaft by suction to specific location outside patient body
Patent Assignee: BONUTTI 2003 TRUST-A (BONU-N); BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (2 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20020082631	A1	20020627	200268	B
US 6835198	B2	20041228	200502	E

US 20020082631
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 20014905 A 20011205; US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 20014905 A 20011205
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 20014905 A 20011205

Alerting Abstract US A1
NOVELTY - A cutting tip (16) is mounted on a flexible drill shaft (14) for cutting tissue. The motion of the shaft moves the cutting tip against the tissue to cut tissue fragments from the tissue. The tissue fragments are removed along the shaft by suction to a location outside the patient body while cutting tissue.
DESCRIPTION - INDEPENDENT CLAIMS are included for:

3. Tissue removing method; and
4. Grafting method of human tissue.

USE - For removing tissue of cartilage, muscle, **fetal**, etc., for tissue grafting (claimed) and also used for removing or breaking stones of kidney, gall bladder and tumors from stomach.
ADVANTAGE - The flexible drill shaft allows the surgeon to guide the cutting tip into various locations within the tissue from one small incision and also allows to cut tissue around arcs or angles. As the cutting tip and drill shaft are small, the device is allowed to be used for endoscopic, arthroscopic, fiberoptic or open surgery. Provides safe and efficient way to collect and reuse a patient's own tissue with fewer complications and less pain.
DESCRIPTION OF DRAWINGS - The figure shows a schematic view of tissue removal system.
14 Flexible drill shaft
16 Cutting tip

3/25/10 (Item 10 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0012713945 *& & Drawing available*
WPI Acc no: 2002-565627/200260
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340;

1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-403322; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551

XRPX Acc No: N2002-447730

Tissue removal apparatus e.g. for bone tissue, has trap to remove tissue fragments cut by cutting tip of drill shaft, and removed by suction out of body during cutting

Patent Assignee: BONUTTI P M (BONU-I)

Inventor: **BONUTTI P M**

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20020055755	A1	20020509	200260	B

US 20020055755

Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 20013996 A 20011115

Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 20013996 A 20011115

Alerting Abstract US A1

NOVELTY - A cutting tip (16) is mounted on a flexible drill shaft (14) made of polymeric or ceramic material, for cutting tissue. A motor (20) transmits motion to the shaft for moving the cutting tip against the tissue to cut the fragments from the tissue. The tissue fragments along the shaft are removed by a trap (28) by suction, to a location outside the body while cutting.

DESCRIPTION - An INDEPENDENT CLAIM is included for tissue removal method.

USE - Used for removing bone tissue, cartilage, muscle, **fetal** tissue, kidney stone, tumor, polyp or tumor, etc.

ADVANTAGE - Since the drill shaft is flexible the surgeon guides the cutting tip into various locations within the tissue by a small percutaneous incision, minimizing damage to skin, muscle and bone and resulting in limited post-operative bleeding and pain.

DESCRIPTION OF DRAWINGS - The figure shows a schematic view of the tissue removal system including a

flexible drill.
14 Flexible drill shaft
16 Cutting tip
20 Motor
28 Trap

3/25/11 (Item 11 from file: 350) **Links**
Fulltext available through: Order File History
Derwent WPIX

0012457410 & & *Drawing available*
WPI Acc no: 2002-403322/200243
Related WPI Acc No: 1992-406998; 1992-407006; 1993-125932; 1993-404771; 1994-092210; 1994-233340; 1994-240674; 1994-293055; 1995-146667; 1995-350397; 1996-238619; 1996-383554; 1997-020009; 1997-099322; 1997-447852; 1997-469887; 1997-558017; 1998-040884; 1998-100214; 1998-144669; 1998-239066; 1998-593885; 1999-130313; 1999-243084; 1999-243093; 1999-443091; 1999-478165; 1999-539487; 2000-115843; 2000-170338; 2000-316553; 2000-429846; 2000-464731; 2000-524078; 2000-531963; 2000-664285; 2001-060243; 2001-111909; 2001-146195; 2001-158464; 2001-225865; 2001-256661; 2001-335217; 2001-373618; 2001-464368; 2001-496417; 2001-513534; 2001-541212; 2001-580208; 2001-625006; 2002-025562; 2002-315057; 2002-382134; 2002-404343; 2002-413208; 2002-425326; 2002-433604; 2002-434608; 2002-507513; 2002-565627; 2002-589815; 2002-627058; 2002-635503; 2002-642396; 2002-664619; 2002-673585; 2002-706046; 2002-711855; 2002-749526; 2003-029812; 2003-057064; 2003-089999; 2003-220849; 2003-247723; 2003-276880; 2003-277284; 2003-278066; 2003-278067; 2003-415342; 2003-416704; 2003-456139; 2003-479353; 2003-540700; 2003-558800; 2003-568878; 2003-596701; 2003-687063; 2003-695887; 2003-720043; 2003-743415; 2003-747318; 2003-754600; 2003-778028; 2003-787950; 2003-874331; 2003-900689; 2004-060591; 2004-179103; 2004-280796; 2004-389208; 2004-389247; 2004-389274; 2004-487398; 2004-517208; 2004-517209; 2004-625134; 2004-634586; 2004-651420; 2004-689912; 2005-010704; 2005-019512; 2005-029413; 2005-056915; 2005-466593; 2005-550885; 2005-618183; 2005-648883; 2005-796407; 2006-115457; 2006-170683; 2006-362313; 2006-567599; 2006-621350; 2006-716854; 2006-796978; 2007-006926; 2007-024680; 2007-025025; 2007-082278; 2007-324700; 2007-511983; 2007-569301; 2007-585308; 2007-891746; 2008-C35145; 2008-C62749; 2008-C75729; 2008-D00551
XRPX Acc No: N2002-316435
Percutaneous tissue removal apparatus for use during endoscopic surgery, removes tissue fragments cut by cutting tip mounted on flexible drill shaft, by performing suction at location outside human body
Patent Assignee: BONUTTI P M (BONU-I)
Inventor: **BONUTTI P M**

Patent Family (1 patents, 1 & countries)

Patent Number	Kind	Date	Update	Type
US 20020029055	A1	20020307	200243	B

US 20020029055
Local Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US

2000483676 A 20000114; US 2001872526 A 20010601
Priority Applications (no., kind, date): US 1990545908 A 19900628; US 1993134914 A 19931012; US 1994353494 A 19941209; US 1996695274 A 19960809; US 1997834835 A 19970411; US 1999323326 A 19990601; US 2000483676 A 20000114; US 2001872526 A 20010601

Alerting Abstract US A1
NOVELTY - Cutting tip (16) made of polymeric or ceramic material, which is mounted on a flexible drill shaft (14), is moved by rotating the shaft using a motor. The cut tissue fragments along the shaft, are removed by suction at a location outside the human body, during cutting.
DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

E. Tissue removal method;
F. Tissue grafting method.

USE - For removal of percutaneous tissues during endoscopic, anthroscopic, fiber optic or open surgeries. Also for removal and grafting of bone tissue, cartilage, muscle, **fetal** tissue, kidney stones in gall bladder, stone or tumor in stomach, polyp or tumor in colon, etc.
ADVANTAGE - Enables to removing only softer inner cancellous bone, as the drill shaft is flexible. Enables cutting tissue at any desired location with less damage to bone, skin and muscle. Enables safe and efficient cutting of tissue.
DESCRIPTION OF DRAWINGS - The figure shows a tissue removal apparatus.
14 Flexible drill shaft
16 Cutting tip

?

Fetal Tissue Engineering: Diaphragmatic Replacement

By Dario O. Fauza, Jennifer J. Marler, Rahul Koka, R. Armour Forse, John E. Mayer, and Joseph P. Vacanti
Boston, Massachusetts

Background/Purpose: Prosthetic repair of congenital diaphragmatic hernia has been associated with high complication rates. This study was aimed at applying fetal tissue engineering to diaphragmatic replacement.

Methods: Fetal lambs underwent harvest of skeletal muscle specimens. Once expanded in vitro, fetal myoblasts were suspended in a collagen hydrogel submitted to controlled radial tension. The construct was then placed in a bioreactor. After birth, all animals underwent creation of 2 diaphragmatic defects. One defect was repaired with the autologous-engineered construct placed in between 2 acellular supporting membranes and the other with an identical construct but without any cells. Each animal was its own control (graft, n = 10). Animals were killed at different time-points postimplantation for histologic examination. Statistical analysis was by analysis of variance (ANOVA).

Results: Fetal myoblasts expanded up to twice as fast as neonatal cells. Hydrogel-based radial tension enhanced construct architecture by eliciting cell organization within the scaffold. No eventration was present in 4 of 5 engineered constructs but in 0 of 5 acellular grafts ($P < .05$). At harvest, engineered constructs were thick and histologically resembled normal skeletal muscle, whereas acellular grafts were thin, floppy, and showed low cell density with increased fibrosis.

Conclusions: Unlike acellular grafts, engineered cellular diaphragmatic constructs are anatomically and histologically similar to normal muscle. Fetal tissue engineering may be a viable alternative for diaphragmatic replacement.

INDEX WORDS: Fetal surgery, tissue engineering, videofetoscopy, congenital diaphragmatic hernia, diaphragm, congenital anomalies, birth defects, fetus, prenatal, neonate, transplantation.

POSTOPERATIVE recurrence rates of congenital diaphragmatic hernia (CDH) have been reported to be between 6% and 75%.[1-7] The majority of those cases occur in children in whom a prosthetic patch was used for repair of the hernia.[1,2,4,5] The main mechanism behind hernia recurrence is believed to be related to normal growth, which is supposed to lead to traction and eventual detachment of the prosthesis, usually at its posteriormedial aspect.[4] Patch disruption is predicted to occur at approximately 18 months of age in most patients, especially if little or no muscle was available for prosthetic attachment at primary repair.[7] Scoliosis, which has been observed in 10% to 12% of cases of CDH, seems to be a risk factor for recurrence in infants that received a prosthesis.[1,8] Repair of CDH with artificial prosthetic patches also has been associated with higher rates of infection, adhesions, and both thoracic and spinal column deformities, when compared with primary repair.[9-11] Acellular bioprosthetic diaphragmatic replacement has been performed in a leporine model but resulted in limited cellularization of the graft by ingrowths from the normal surrounding tissue.[12]

This study was aimed at (1) applying the concept of autologous fetal tissue engineering (Fig 1) as a means of building cellular bioprosthetic diaphragmatic constructs, (2) analyzing the effects of current tissue engineering techniques on fetal myoblasts, and (3) comparing the progress of both cellular and acellular bioprosthetic diaphragmatic grafts with time, postimplantation after birth.

MATERIALS AND METHODS

The Harvard Medical School animal management program is sanctioned by the American Association for the Accreditation of Laboratory Animal Care (AAALAC, file # 000009) and meets National Institutes of Health standards as set forth in the Guide for the Care and Use of Laboratory Animals (National Research Council Publication, Revised 1996).

Maternal and Fetal Surgical Manipulation

Time-dated pregnant ewes at 95 to 105 days' gestation were anesthetized with 2% to 4% Halothane (Halocarbon Laboratories, River Edge, NJ). They received 1 g of cefazolin (G.C. Hanford, Syracuse,

Dario O. Fauza was supported by grants from the Harvard Medical School's Center for Minimally Invasive Surgery and the United States Surgical Corporation. Jennifer J. Marler was supported by a Faculty Research Grant from the American College of Surgeons and a Scholars-in-Medicine Award from Harvard Medical School. Both authors contributed equally to the study.

From the Harvard Center for Minimally Invasive Surgery and the Departments of Surgery, Children's Hospital and Harvard Medical School, Boston, MA.

Presented at the 31st Annual Meeting of the American Pediatric Surgical Association, Orlando, Florida, May 25-29, 2000.

This research was supported by grants from the United States Surgical Corporation and the Plastic Surgery Educational Foundation.

Address reprint requests to Joseph P. Vacanti, MD, Massachusetts General Hospital, 55 Fruit St, Warren 1157, Boston, MA 02114.

0022-3468/01/3601-0025$03.00/0
doi:10.1053/jpsu.2001.20034

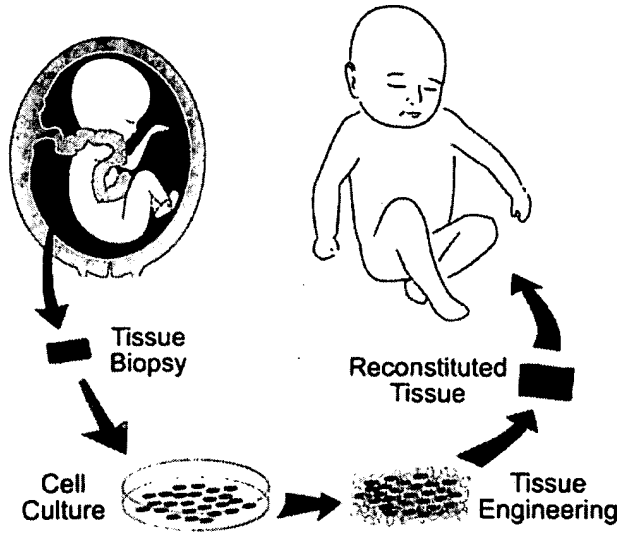

Fig 1. The concept of autologous fetal tissue engineering: minimally invasive harvest of fetal tissue, which then is engineered in vitro while pregnancy is allowed to continue, so that a newborn with a prenatally diagnosed birth defect can benefit from having autologous, expanded tissue promptly available for definitive surgical treatment in the neonatal period.

NY) intravenously before surgical manipulation. The bicornuate uterus was then exposed through a median longitudinal laparotomy. If twin pregnancy was present, surgical manipulation was performed only in 1 fetus. Fetal lambs (n = 5) underwent either open or videofetoscopic harvest of a skeletal muscle specimen no larger than 1.5 × 1.0 × 1.0 cm, from the posterior aspect of the neck or a hind limb, which was placed immediately in cation-free Hanks' Balanced Salt Solution (Sigma Chemical, St Louis, MO) on ice. If videofetoscopic access to the amniotic cavity was established, semiflexible, balloon-tipped cannulas (Marlow Surgical Technologies, Willoughby, OH) were introduced in the uterus through 3 ports (1 of 10 mm and 2 of 5 mm in size). Videofetoscopic manipulation was performed either under continuous warmed saline amnioinfusion or with medical air as working media ("floating fetus"). A 30°, 5-mm telescope (Karl Storz Endoscopy, Los Angeles, CA), along with 2-mm and 5-mm endoscopic graspers and 2-mm and 5-mm endoscopic shears were used (all from United States Surgical Corporation [USSC], Norwalk, CT). At the end of either type of harvesting procedure (minimally invasive or open), the amniotic fluid, which previously had been partially removed and kept at 37°C, was reinfused into the amniotic cavity, together with 500 mg of Cefazolin. If the procedure was open, the gestational membranes and uterine wall were closed in 1 layer with a reusable TA 90-mm. Titanium surgical stapler (USSC, Norwalk, CT). If it was videofetoscopic, the uterine ports were closed with 4-0 synthetic absorbable Glycomer 631 (Biosyn, USSC, Norwalk, CT) in double-running fashion. The mother's abdomen was closed in layers. On the first postoperative day, the ewes received 1.2 million units of Benzatin penicillin intramuscularly (Wyeth Laboratories, Philadelphia, PA).

Cell Manipulation

Cell culture. After mincing, the skeletal muscle specimens were digested with a collagenase/dispase mixture (1% Type II collagenase [Worthington Biochemical, Lake View, NJ], 2.4 U Dispase II [Boerhinger, Mannheim, Germany], 2.5 mmol/L $CaCl_2$) for 30 minutes in a 5% CO_2 incubator at 37°C. After trituration and passage through a 70-μm mesh, the cells were spun down, counted and plated at a density of 3 million cells per 150 cm^2 in flasks that had been precoated overnight with laminin (Sigma Chemical, St Louis, MO), at 5 μg/mL in Dulbecco's Phosphate Buffered Saline (PBS; Sigma Chemical, St Louis, MO), at 4°C. Cells were fed daily with myoblast medium, composed of Ham's F10 medium (Sigma Chemical) containing 20% fetal bovine serum (Sigma Chemical), 3 ng/mL basic fibroblast growth factor (Promega, Madison, WI), glutamine, penicillin, and fungizone (all the latter from Gibco, Grand Island, NY), in a 95% humidified, 5% CO_2 chamber at 37°C. Flasks were split daily at a ratio of 1:3 into additional laminin-coated plates and subsequently into roller bottles. When 10 roller bottles of cells were available (a yield of approximately 100 million), the cells were trypsinized (Sigma Chemical) placed in serum-free Ham's F10 medium, washed twice, counted, and spun down.

To ascertain myoblast identity, immunocytochemical staining was done for desmin, a marker of myogenicity. Cells were plated in LabTek tissue culture chamber slides (Fisher Scientific, Pittsburgh, PA). They were fixed with 4% neutral buffered formaldehyde (Sigma Chemical) for 10 minutes, rinsed in phosphate-buffered saline (PBS), and fixed with 100% methanol (Sigma Chemical) for 10 minutes. They were rinsed with a "blocking solution" that consisted of 2% horse serum (Sigma Chemical) and 0.5% Triton (Sigma Chemical) in PBS and incubated in this solution for 30 minutes. They were incubated overnight in a 1:400 antidesmin mouse monoclonal ascites (Sigma Chemical), rinsed with blocking solution 3 times and incubated in a goat-anti-mouse FITC secondary antibody (Sigma Chemical) for 30 minutes. After 3 rinses in blocking solution, the slides were mounted in DAPI fluorescence medium (Vector Labs, Burlingame, CA) and viewed with a Zeiss fluorescence microscope (Zeiss, Germany).

Construct assembly. The cell pellet was resuspended in 10 mL of a collagen hydrogel (1.7 mg/mL collagen [ICN, Costa Mesa, CA], 17% Matrigel [Collaborative Biomedical, Madison, WI], pH 7.2) that was reconstituted with 10× Ham's F10 medium and kept at 4°C to maintain it in its liquid state. The gel was poured into a circular mold consisting of a round wire mesh 85 mm in diameter, which had a central opening 45 mm in diameter and a sheet of silicone at its base. The gel was then covered with a circular silicone elastomer block to ensure that the mesh was impregnated evenly with gel and placed in an incubator at 37°C for 30 minutes. During this period, the gel became stiff. The placement of the seeded collagen hydrogel into this circular mold provided continuous radial tension to the construct. The elastomer block was removed, and the mesh containing the construct was transferred to a bioreactor. The bioreactor consisted of a large spinner flask in a 5% CO_2 incubator, which contained a framework to hold the mesh, myoblast medium, and

Fig 2. Abdominal view of both forms of repair of the surgically created diaphragmatic defects. The lighter patch contains a cellular, tissue-engineered construct, whereas the darker one contains an identical scaffold, but without any cells.

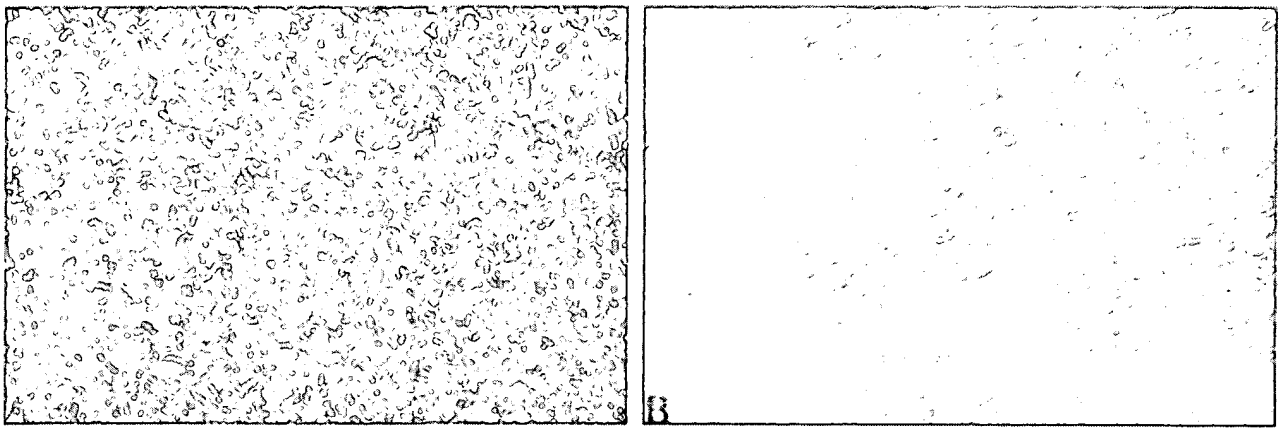

Fig 3. Phase microscope view of myoblasts seeded within the collagen hydrogel scaffold. (A) Before controlled mechanical stretch of the scaffold. (B) Continuous radial tension elicited cell orientation in parallel to the tension vectors within the collagen scaffold, thus enhancing construct architecture.

a magnet to maximize perfusion of the construct. The medium was changed twice weekly.

The construct was maintained in the bioreactor until the time of implantation into the animal, at which time it was washed for 4 hours with serum-free Ham's F10, placed in Hanks' Balanced Salt Solution, and brought to the operating room. Control gels were created by pouring the collagen hydrogel into the same molds and warming them at 37°C to result in cross-linkage.

Neonatal Manipulation

Surgery. Normal delivery was allowed. Eight to 35 days after birth, the newborns were anesthetized with 1.5% to 3.5% Isoflurane (Abbott Laboratories, North Chicago, IL). Animals underwent a left subcostal laparotomy and creation of 2 posterior-lateral left diaphragmatic defects, each of approximately 5 cm in diameter. One defect was repaired with the autologous, engineered construct placed in between 2 layers (one on the thoracic side and the other on the abdominal side of the diaphragmatic defect) of acellular small intestine submucosa (SIS), whereas the other was repaired with an identical construct but without any cells, also in between 2 layers of SIS. Therefore, a total of 10 grafts were implanted, with each animal as its own control. Interrupted sutures of 5-0 monofilament polypropylene (Surgipro, USSC, Norwalk, CT) were used to attach both SIS layers to the edges of each diaphragmatic defect, with the collagen hydrogel simply placed in between the 2 SIS layers (Fig 2). Local omentum was used to cover both repaired defects by loosely attaching it to the diaphragm, around the edges of the implants, with 4 to 6 simple cardinal stitches of 5-0 monofilament polypropylene.

During laparotomy closure, air was drained from the pleural cavities through a multiperforated chest tube, which was removed at the end of the procedure. On the first postoperative day, all newborns received one dose of 0.6 million units of Benzatin Penicillin intramuscularly.

Follow-up. Animals were killed at 3, 8, 9, 10, and 12 weeks postimplantation, when diaphragmatic constructs were harvested for histologic analysis.

Histologic Analysis

Construct specimens were immersed in 10% buffered formalin (Stephens Scientific, Riverdale, NJ) on retrieval and submitted to regular H&E and Masson's Trichrome processing 24 to 48 hours postharvesting. Microscopic analysis was performed at 10×, 25× and 100× magnification using a Zeiss (Zeiss, Germany) laboratory light microscope.

Statistical Analysis

Statistical analysis was performed by analysis of variance (ANOVA) and the Scheffe-f test at 95% confidence limit. *P* values of less than .05 were considered significant.

RESULTS

Fetal and neonatal survival rates were 100%. There were no perioperative complications with either harvest-

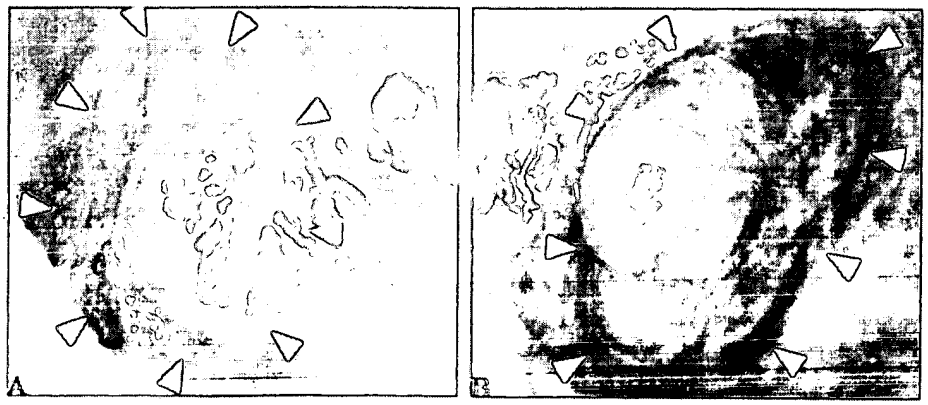

Fig 4. Typical thoracic view of both forms of diaphragmatic repair at 8 weeks postimplantations. Arrows point to the edges of each bioprosthesis. (A) Engineered construct (notice near-normal appearance and absence of eventration); (B) Acellular construct (notice visualization of omental fat through the construct and eventration).

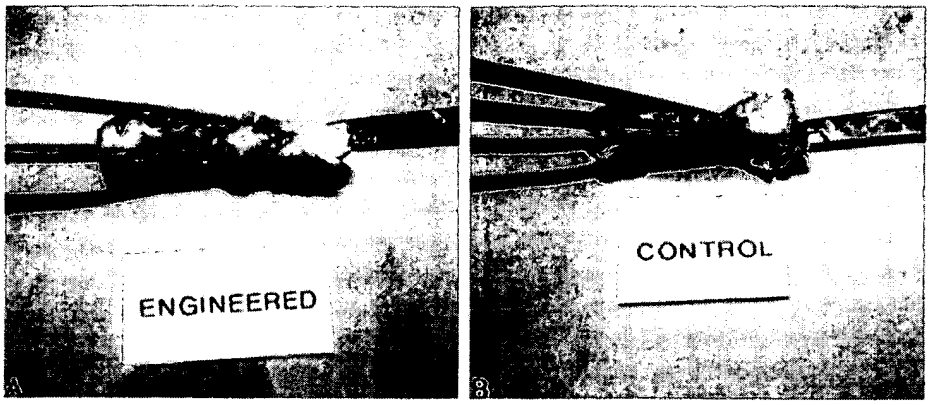

Fig 5. Gross views of both types of bioprosthesis after harvest and fixation with Formalin. Engineered constructs (A) appeared much thicker than acellular grafts (B).

ing method (open or videofetoscopic), or involving construct implantations. Fetal myoblasts expanded at faster rates than have been reported from neonatal cells (up to 2-fold).[13] Desmin immunocytochemistry before construct assembly showed that approximately 80% of isolated cells were myogenic in identity. The remaining cells had a fibroblastic appearance. Continuous radial tension enhanced construct architecture by eliciting cell orientation in parallel to the tension vectors within the collagen scaffold (Fig 3). At harvest, eventration was present in all acellular grafts, but in only 1 engineered construct ($P < .05$; Fig 4). Despite accelerated animal growth, no recurrence was observed in either group, with both the SIS and the collagen scaffold showing valuable elasticity. Engineered constructs appeared thick and histologically resembled normal skeletal muscle, whereas acellular grafts were thin, floppy, and showed low cell density and increased fibrosis (Figs 5 and 6).

DISCUSSION

At the current stage of fetal intervention, the application of the concept of autologous fetal tissue engineering for treatment of birth defects could only be justified in life-threatening congenital anomalies. Preterm labor (mostly), as well as other general complications and risks of fetal surgery would render other applications of this concept ethically unacceptable, at least for now. In CDH, the diaphragmatic defect per se is not life threatening and, hence, would not be eligible for repair via this concept for the time being. However, one could justify the harvest of a very small specimen from a superficial skeletal muscle of a fetus that is being submitted to tracheal occlusion for treatment of pulmonary hypoplasia associated with CDH. Videofetoscopic fetal tracheal occlusion is establishing itself as a valid and safe alternative for a select group of fetuses with CDH, and such a harvest should not add sizeable risk to the procedure.[14]

As hereby shown, unlike acellular grafts, engineered cellular diaphragmatic constructs are anatomically and histologically similar to normal muscle. However, despite the clear advantages of an autologous-engineered construct over an acellular bioprosthesis, this experiment should be viewed as an initial study. A number of

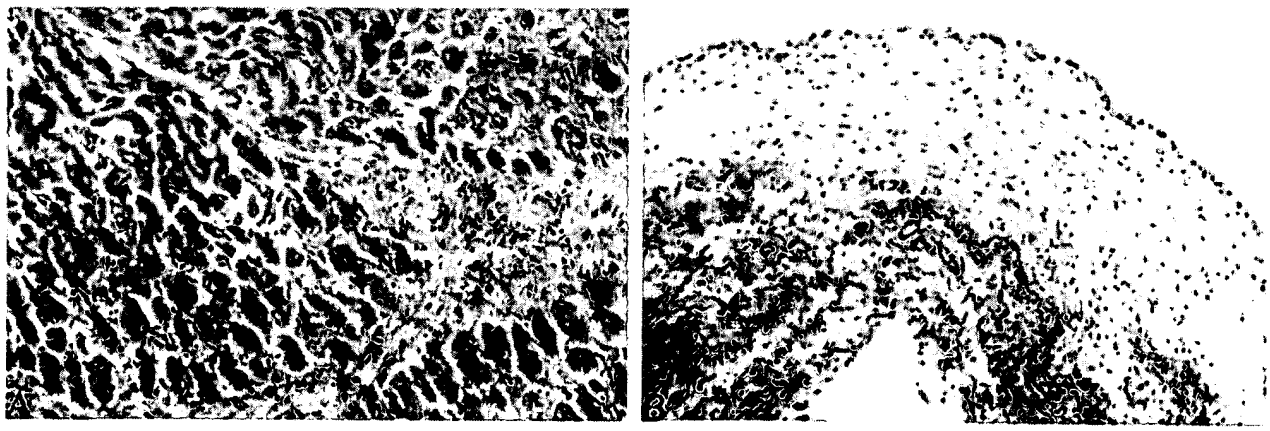

Fig 6. Microscopic views of midimplant areas from a tissue-engineered construct (A) and an acellular construct (B), 60 days postoperatively. Notice typical histologic characteristics of skeletal muscle, permeated by omental ingrowths in (A). A thin, fibrotic tissue, with low cell density and covered by a mesothelial layer on its pleural side is observed in (B). (H&E, original magnification ×100.)

different pieces of information are still needed before this technique can be translated into clinical use. Longer periods of time between construct implantation and harvest should yield data on possible nerve ingrowths and functional aspects of the construct and on eventual complication rates. We must also emphasize that, for technical reasons, all implants of the current study were attached to the diaphragm predominantly at its posterior aspect, which offers some mechanical support from the adjacent posterior and caudal rib cage. Although there were significant differences in the eventration rates between both groups, it would be necessary to study the behavior of even larger constructs placed in areas of the diaphragm with less mechanical support, or none at all, such as its dome. Likewise, other methods of scaffold engineering, including its composition and design, should be explored. Not only can different scaffolds provide different degrees of tensile strength until the new tissue is fully incorporated by the host, their composition also can influence the extent of differentiated function and proliferation of the cells seeded onto them.[15]

The course of skeletal muscle differentiation in vitro is well established. In many ways, it follows the in vivo sequence, including the fusion of myoblasts into contractile myofibers expressing skeletal muscle-specific genes under appropriate tissue culture conditions.[13] During organogenesis, mechanical tension is an important organizing force within skeletal muscle tissue. The application of in vivo–like mechanical tension to differentiating myoblasts in vitro, as used in the current study, has been reported previously to lead to stronger organ-like muscle structures capable of directed functional work.[16] However, other external stimuli also should be explored as a means to further enhance bioengineered muscle construct architecture. For example, the application of electromagnetic fields has been shown to induce assorted responses in different biological systems, both in vivo and in vitro, including nerve regeneration, increased protein and DNA synthesis, elevation of intracellular Ca^{+2} concentration and cytoskeletal reorganization.[17-21]

Although all the improvements and further studies mentioned above should be pursued before clinical application, the current data suggest that autologous fetal myoblast tissue engineering can be a viable and potentially improved alternative for diaphragmatic replacement after birth.

ACKNOWLEDGMENTS

The authors are indebted to Jeffrey Pettit for his excellence in laboratory assistance.

REFERENCES

1. Lund DP, Mitchell J, Kharasch V, et al: Congenital diaphragmatic hernia: The hidden morbidity. J Pediatr Surg 29:258-62; discussion 262-264, 1994

2. Van Meurs KP, Robbins ST, Reed VL, et al: Congenital diaphragmatic hernia: Long-term outcome in neonates treated with extracorporeal membrane oxygenation. J Pediatr 122:893-899, 1993

3. West KW, Bengston K, Rescorla FJ, et al: Delayed surgical repair and ECMO improves survival in congenital diaphragmatic hernia. Ann Surg 216:454-460; discussion 460-462, 1992

4. Lally KP, Paranka MS, Roden J, et al: Congenital diaphragmatic hernia. Stabilization and repair on ECMO. Ann Surg 216:569-573, 1992

5. Bianchi A, Doig CM, Cohen SJ: The reverse latissimus dorsi flap for congenital diaphragmatic hernia repair. J Pediatr Surg 18:560-563, 1983

6. Cohen D, Reid IS: Recurrent diaphragmatic hernia. J Pediatr Surg 16:42-44, 1981

7. Atkinson JB, Poon MW: ECMO and the management of congenital diaphragmatic hernia with large diaphragmatic defects requiring a prosthetic patch. J Pediatr Surg 27:754-756, 1992

8. Falconer AR, Brown RA, Helms P, et al: Pulmonary sequelae in survivors of congenital diaphragmatic hernia. Thorax 45:126-129, 1990

9. D'Agostino JA, Bernbaum JC, Gerdes M, et al: Outcome for infants with congenital diaphragmatic hernia requiring extracorporeal membrane oxygenation: the first year. J Pediatr Surg 30:10-15, 1995

10. Cullen ML: Congenital diaphragmatic hernia: Operative considerations. Semin Pediatr Surg 5:243-248, 1996

11. Greenholz SK: Congenital diaphragmatic hernia: An overview. Semin Pediatr Surg 5:216-223, 1996

12. Housley HT, Graf JL, Gibbs DL, et al: Acellular diaphragmatic replacement in Weanling rabbits Twenty-Eighth Annual Meeting of the American Pediatric Surgical Association, Naples-FL, 1997

13. Vandenburgh H, Del Tatto M, Shansky J, et al: Tissue-engineered skeletal muscle organoids for reversible gene therapy. Hum Gene Ther 7:2195-2200, 1996

14. Harrison MR, Mychaliska GB, Albanese CT, et al: Correction of congenital diaphragmatic hernia in utero IX: Fetuses with poor prognosis (liver herniation and low lung-to-head ratio) can be saved by fetoscopic temporary tracheal occlusion. J Pediatr Surg 33:1017-1022; discussion 1022-1023, 1998

15. Mooney D, Hansen L, Vacanti J, et al: Switching from differentiation to growth in hepatocytes: Control by extracellular matrix. J Cell Physiol 151:497-505, 1992

16. Vandenburgh HH, Swasdison S, Karlisch P: Computer-aided mechanogenesis of skeletal muscle organs from single cells in vitro. Faseb J 5:2860-2867, 1991

17. Sisken BF, Smith SD: The effects of minute direct electrical currents on cultured chick embryo trigeminal ganglia. J Embryol Exp Morphol 33:29-41, 1975

18. Bourguignon GJ, Bourguignon LY: Electric stimulation of protein and DNA synthesis in human fibroblasts. Faseb J 1:398-402, 1987

19. Cho MR, Thatte HS, Lee RC, et al: Reorganization of microfilament structure induced by ac electric fields. Faseb J 10:1552-558, 1996

20. Cho MR, Thatte HS, Silvia MT, et al: Transmembrane calcium influx induced by ac electric fields. Faseb J 13:677-683, 1999

21. Onuma EK, Hui SW: Electric field-directed cell shape changes, displacement, and cytoskeletal reorganization are calcium dependent. J Cell Biol 106:2067-2075, 1988

Discussion

P. Glick (Buffalo, NY): The diaphragmatic defects that we are dealing with clinically are much, much larger than what you showed us there, and so based on the tissue strength and the ability to bring in a blood supply, what is the limitation on being able to construct artificial bioengineered diaphragms that we are going to be able to use to replace the entire diaphragm, but that usually is the situation that we are in.

D.O. Fauza (response): The answer to this question is to be determined, but I can tell you that the area of scaffold engineering is very vast. We literally have dozens of different scaffolds that we can explore. The importance of that study was to show that delivering cells to a bioprosthetic graft made a difference. We have to have cells, not only a bioprosthetic graft. Which scaffold we use is to be determined. I agree with you we should have much larger defects before we go into clinical application, and we plan on doing that. We just wanted to see whether engineering something, giving cells, instead of just a bioprosthetic graft, made a difference.

P. Glick: But from all the work in your laboratory what are going to be the limitations on taking a bioengineered graft, putting it into an animal or human that is going to require picking up a blood supply? The center of the graft is going to be relatively ischemic, so how big can grafts be before . . .

D.O. Fauza (response): The answer is, I do not know. What I can tell you is some scaffolds hold nutrients for a long time within them so nutrients could be given to the cells for a long time. The problem is the gas exchanged and whether we can devise perhaps an in vivo bioreactor in which you have gas exchange, pretty much like you saw in the incubator, but coming out of lines out of the patient for a while. It is something to be explored, but it is a very important point.

J.-M. Laberge (Montreal, Quebec): One thing I was wondering is if you inverted the position of your graft just to make sure that one side is not covered by the spleen more than the other side, or did you always use the same two positions?

D.O. Fauza (response): We did invert, and it did not make any difference because the omentum was right in between the spleen and the diaphragmatic defect. We did invert, and I did not see any difference with that.

D. Kays (Gainesville, FL): How long does it take to grow this, and how many cells do you need? Do you see a chance in the future that we could just do a core needle biopsy or something of tissue rather than taking out a chunk like you did with the trocar?

D.O. Fauza (response): Yes, I do. I do see that possibility, and I also see the possibility of a bank of fetal cells. We had to throw cells away. They grew too quickly, much earlier than birth. How many cells you need depends on the scaffold you use and the size of the defect you want to repair, but what you said is very much true. I think that ultrasound-guided biopsy is a possibility, not to mention what I just said about a bank of fetal cells and maybe not even the need for a biopsy, although I think it would be preferable because you are talking about autologous tissue.

Videofetoscopically Assisted Fetal Tissue Engineering: Skin Replacement

By Dario O. Fauza, Steven J. Fishman, Kathryn Mehegan, and Anthony Atala
Boston, Massachusetts

Background/Purpose: Treatment of several congenital anomalies is frequently hindered by lack of enough tissue for surgical reconstruction in the neonatal period. The purposes of this study were (1) introduction of a novel concept in perinatal surgery, involving minimally invasive harvest of fetal tissue, which is then processed through tissue engineering techniques in vitro while pregnancy is allowed to continue, so that, at delivery, the newborn can benefit from having autologous, expanded tissue promptly available for surgical implantation at birth; (2) analysis of the progress of an engineered fetal skin graft with time, after implantation in the neonate; and (3) study of the effects of current tissue engineering techniques on fetal keratinocytes and fetal dermal fibroblasts.

Methods: Ten 90- to 95-day-gestation fetal lambs underwent surgical creation of two large paramedian excisional skin defects on the posterior body wall. Subsequently, fetal skin specimens no larger than 1.5 × 1.5 cm were videofetoscopically harvested. Fetal keratinocytes and dermal fibroblasts were then separately cultivated and expanded in vitro for 45 to 50 days, resulting in a total of approximately 250 to 300 million cells. Seven to 10 days before fetal delivery, all cells were seeded in two layers on a 16 to 20-cm^2, 3-mm thick biodegradable polyglycolic acid polymer matrix. One to 4 days after delivery, the autologous engineered skin was implanted over one of two previously created skin defects. The second skin defect region received an absorbable polymer scaffold without cells as a control. If necessary, the original skin wounds were further amplified before implantation. Each animal provided at least one time-point for histological analysis of both types of repair through excisional biopsies performed at weekly intervals, up to 8 weeks postimplantation. Normal skin specimens were also used as controls.

Results: Fetal and neonatal survival rates were 100%. Based on previous postnatal skin engineering studies, fetal dermal fibroblasts multiplied significantly faster in vitro (approximately fivefold) than expected. Fetal keratinocytes multiplied at expected postnatal rates. The engineered grafts induced faster epithelization of the wound (partial at 1 week and complete between 2 and 3 weeks postoperatively) than did the acellular ones (partial at 3 weeks and complete between 3 and 4 weeks postoperatively). Analysis of skin architecture showed a higher level of epidermal organization and less dermal scarring in the wounds that received the engineered, cell-implanted polymer scaffold.

Conclusions: (1) Videofetoscopically assisted fetal tissue engineering is a viable method for obtaining expanded autologous tissue for prompt surgical reconstruction at birth. (2) Fetal skin can be expanded and engineered in vitro at faster rates than expected postnatally, with current tissue engineering techniques. (3) Engineered autologous fetal skin induces a faster and more organized healing of neonatal skin defects than that observed with second intention. This concept may prove useful for the treatment of certain human neonatal conditions such as giant neoplasias, ectopia cordis, and other body wall defects.

INDEX WORDS: Fetal surgery, videofetoscopy, tissue engineering, skin, transplantation.

CONGENITAL ANOMALIES, by definition, involve loss and/or malformation of tissues or organs. The definitive treatment of many congenital anomalies at birth is often limited by the scarce availability of normal tissues or organs, either in an autologous or allologous fashion. The well-known severe donor shortage observed in practically all areas of transplantation is even more critical during the neonatal period. Furthermore, autologous grafting is frequently not an option in newborns because of donor site size limitations.

One of the purposes of the present study was to introduce a novel concept in perinatal surgery, involving minimally invasive harvest of fetal tissue, which is then engineered in vitro while pregnancy is allowed to continue, so that an infant with a prenatally diagnosed birth defect can benefit from having autologous, expanded tissue promptly available for surgical implantation in the

From the Harvard Center for Minimally Invasive Surgery and the Departments of Surgery and Urology, Children's Hospital and Harvard Medical School, Boston, MA

Presented at the 28th Annual Meeting of the American Pediatric Surgical Association, Naples, Florida, May 18-21, 1997.

This research was supported in part by a grant from American Medical Systems, Inc, and the United States Surgical Corporation.

Address reprint requests to Anthony Atala, MD, Children's Hospital, Hunnewell 3, 300 Longwood Ave, Boston, MA 02115.

0022-3468/98/3302-0040$03.00/0

neonatal period. Skin was the tissue selected for this introductory experiment. Other aims were the analysis of the progression of an engineered fetal skin graft with time, after implantation in the neonate, as well as the study of the efficacy of current tissue engineering techniques on fetal keratinocytes and fetal dermal fibroblasts.

MATERIALS AND METHODS

The Harvard Medical School animal management program is accredited by the American Association for the Accreditation of Laboratory Animal Care (AAALAC-file # 000009) and meets National Institutes of Health standards as set forth in the Guide for the Care and Use of Laboratory Animals (National Research Council Publication, Revised 1996).

Fetal Surgical Manipulation

Time-dated pregnant ewes at 90 to 95 days' gestation were anesthetized with 2% to 4% halothane (Halocarbon Laboratories, River Edge, NJ), after induction with 15 mg/kg of ketamine (Parke-Davis Co, Morris Plains, NJ) intramuscularly. They received 1 g of cefazolin (BMH Ltd, Philadelphia, PA, for Eli Lilly and Co, Indianapolis, IN) intravenously. Ten fetal lambs underwent open surgical creation of two large paramedian excisional skin defects on the posterior body wall (Fig 1). At the end of the procedure, the amniotic fluid, which had been previously removed and kept at 37°C, was reinfused in the amniotic cavity, together with 500 mg of cefazolin. The gestational membranes and uterine wall were then closed in one layer with a TA 90-mm Titanium surgical stapler (United States Surgical Corp [USSC], Norwalk, CT).

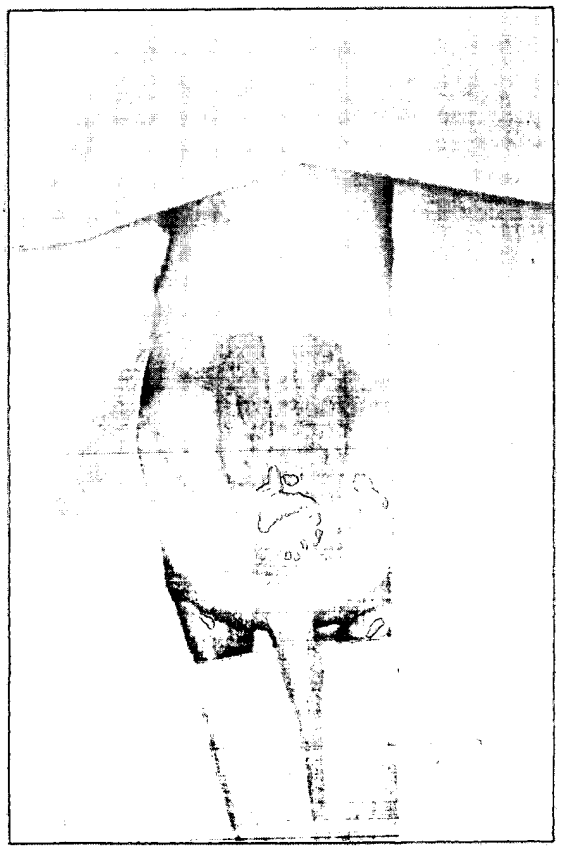

Fig 1. The posterior body wall of a fetal lamb with two surgically created paramedian skin defects.

Subsequently, videofetoscopic access to the amniotic cavity was established. Semiflexible, balloon-tipped cannulas (Marlow Surgical Technologies, Inc, Willoughby, OH) were introduced through three ports (one of 10 mm and two of 5 mm in size). Two different intraamniotic working media were employed. In the first five animals, videofetoscopic manipulation was performed under continuous warmed saline amnioinfusion; in the last five, medical air was used. Fetal skin specimens no larger than 1.5 × 1.5 cm were harvested from the abdominal area. A 5-mm, 30° scope (Karl Storz Endoscopy-America, Inc, Los Angeles, CA), as well as 2-mm endograsps, 2-mm endoshears, and 10-mm titanium endoclips for hemostasis of the harvested area (all from USSC) were used. The uterine ports were closed with 4-0 synthetic absorbable Glycomer 631 (Biosyn, USSC) in double-running fashion. The mother's abdomen was closed in layers. On the first postoperative day, the ewes received 1.2 mu of benzatin penicillin intramuscularly (Wyeth Laboratories, Inc, Philadelphia, PA). All ewes remained at our veterinary facilities after the surgical procedures. Normal delivery was allowed.

Cell Manipulation

The epidermal and dermal layers of the fetal skin specimens harvested were surgically detached from each other and processed separately.

Cell culture. Dermal fibroblasts were further isolated by cutting the dermal specimens into fragments of approximately 0.5 mm in diameter. The explants were plated on a 10 cm culture dish and maintained and expanded with Dulbecco's Modified Eagles Medium (DMEM, Sigma Chemical Co, St Louis, MO) supplemented with 10% fetal calf serum (Biowhittaker, Inc, Walkersville, MD) in a 95% humidified, 5.0% CO_2 chamber at 37°C.

Keratinocytes were fragmented in a similar fashion. The explants were plated on a 10-cm culture dish and maintained and expanded with serum-free keratinocyte growth medium containing 5 ng/mL of epidermal growth factor and 50 μg/mL of bovine pituitary extract (Keratinocyte SFM, Gibco BRL, Life Technologies, Grand Island, NY) in the same chamber described above.

Both dermal fibroblasts and keratinocytes were independently expanded in vitro for 50 to 55 days, until reaching an approximate density of 1.3×10^7 cells/cm^2.

Cell delivery. The cell delivery vehicle consisted of unwoven sheets of polyglycolic acid polymer with a density of 58 mg/mL and a fiber diameter of 15 μm. The mesh had a greater than 95% porosity before seeding and was sterilized by ethylene oxide. The scaffold was designed to degrade via hydrolysis within 6 to 8 weeks after implantation.

Ten days before implantation in vivo, the dermal fibroblasts were seeded on a 16 to 20 cm^2, 3-mm thick polyglycolic acid polymer scaffold (Fig 2). Three days later, the keratinocytes were seeded on the same polymer, over the dermal fibroblasts. The keratinocyte/dermal fibroblast bilayer was left in culture in Dulbecco's modified eagles medium (DMEM) supplemented with 10% fetal calf serum for approximately 1 week until implantation on the newborn animals.

Neonatal Surgical Manipulation

One to 4 days after birth, the newborns were anesthetized with 1.5% to 3.5% isoflurane (Abbott Laboratories, North Chicago, IL), after induction with 15 mg/kg of ketamine intramuscularly. They received 100 mg/kg of cefazolin intravenously. The autologous-engineered skin was implanted over one of the two previously created skin defects. Its borders were sutured to the wound edges with 3-0 synthetic absorbable Lactomer 9-1 (Polysorb, USSC) in simple running fashion (Fig 3). The other skin defect region similarly received an equal-sized absorbable

Fig 2. Phase microscope view of fetal dermal fibroblasts seeded on a 3-mm thick biodegradable polyglycolic acid polymer matrix. Because of the thickness of the matrix and the high number of cells, the latter are visible only at the periphery of the scaffold, surrounding polymer fibers. (Original magnification ×100.)

polymer scaffold, but without any cells, which served as a control (Fig 3). Because of the well-known enhanced healing abilities of the fetus, in many animals the original skin wounds had to be further amplified to accommodate the polymer matrices. In a few animals the wounds were completely healed at birth, and the defects had to be reopened before implantation. On the first postoperative day, the newborns received 0.6 mu of benzatin penicillin intramuscularly.

Each newborn provided at least one time-point for histological analysis of both types of repair through excisional biopsies performed under general anesthesia at weekly intervals, up to 8 weeks postimplantation. Normal skin specimens were also used as controls. All mothers and respective newborns remained at our veterinary facilities until 2 months after the implantations, when they received Somlethal euthanasia solution intravenously (J.A. Webster, Inc, Sterling, MA).

Histological Analysis

Normal skin and skin graft specimens were immersed in 10% buffered formalin solution (Stephens Scientific, Riverdale, NJ) on retrieval and submitted to regular Hematoxilin-Eosin processing 24 to 48 hours postharvesting. Microscopic analysis was performed at 25× and 100× magnification using a Zeiss (Zeiss, Germany) laboratory light microscope.

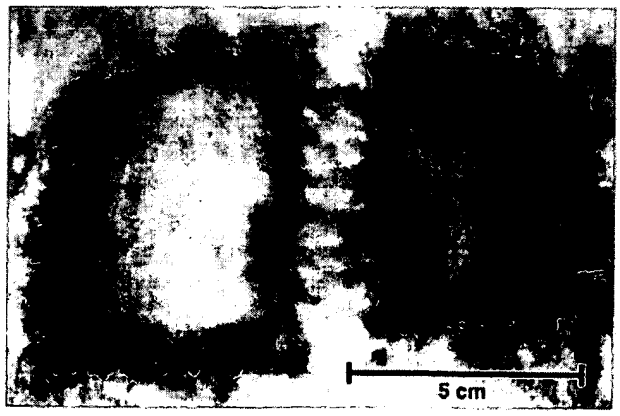

Fig 3. Two biodegradable scaffolds (engineered skin on left, acellular polymer on right) implanted on the posterior body wall of a newborn animal.

RESULTS

Both fetal and neonatal survival rates were 100%. There were no surgical complications. Based on previous skin engineering studies,[1-6] fetal dermal fibroblasts multiplied significantly faster in vitro (approximately fivefold) than cells harvested postnatally. Fetal keratinocytes multiplied at expected postnatal rates.

The engineered autologous skin grafts induced faster epithelization of the wound (partial at 1 week and complete between 2 and 3 weeks postoperatively) than did the acellular ones (partial at 3 weeks and complete between 3 and 4 weeks postoperatively, Fig 4). Time-matched histological analysis of skin architecture showed a higher level of epidermal/dermal organization, richer vascularization, and less dermal scarring in the wounds that received the engineered skin, compared with those that received the acellular matrices (Fig 4). Normal skin

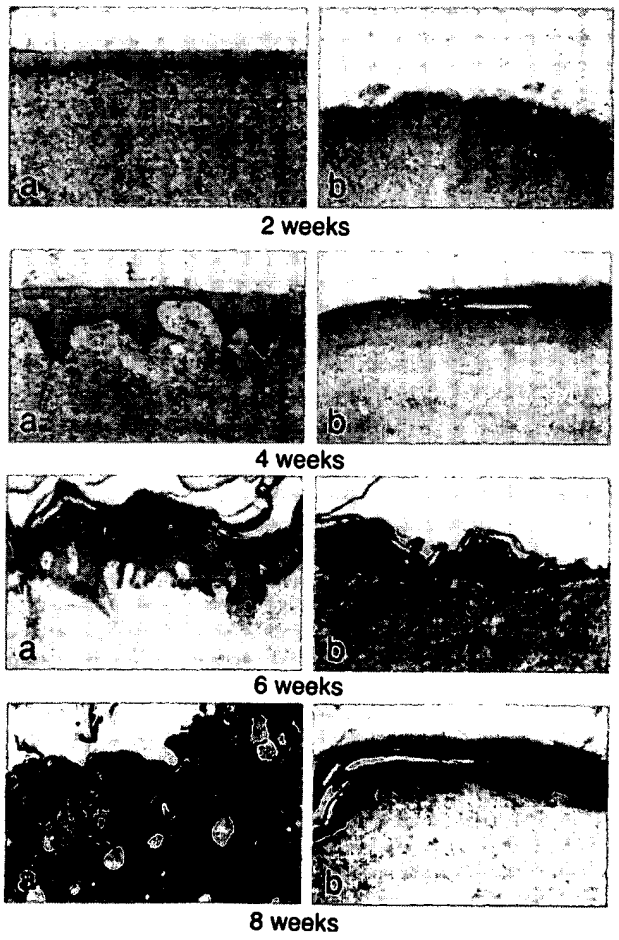

Fig 4. Comparative neoskin histology specimens from engineered (a) and acellular (b) sites at different times postimplantation, in weeks. Notice the faster epithelization time and higher level of organization of the engineered specimens. (H&E, original magnification ×100.)

annexes (Fig 5) were not observed in any grafted area during the period studied, although some areas that received engineered skin showed an architectural pattern compatible with ongoing adnexal development at 8 weeks postimplantation (Fig 4).

DISCUSSION

Several modified methods of tissue and organ transplantation have been introduced in the last few decades as attempts to minimize problems related to scarce donor availability and graft rejection. For skin replacement, those "alternative" methods include the use of synthetic dermal composites associated with epidermal grafts,[7-11] autologous cultured grafts,[1-6] cryopreserved allografts,[5,12,13] and allogeneic-syngeneic cultured grafts.[14,15] Each of these methods have their own disadvantages. With autologous cultured grafts, the most relevant shortcoming is the long time necessary to obtain sufficient amount of graftable sheets needed for wound coverage.[1-6]

The concept introduced in the present study overcomes the time limitations of autologous transplantation. After fetal harvest, the time needed to engineer an autologous graft is parallel to the remainder of gestation and, hence, not at all a limiting factor. Moreover, there is usually an inverse relationship between donor age and cell growth rate in culture, which also applies to the skin.[16-18] The fact that fetal cells were used in our experiment maximized this principle. as demonstrated by the high expansion rate that we observed with the fetal dermal fibroblasts.

We used control wounds covered with the synthetic matrix devoid of cells to ensure that dermal/epidermal regeneration was not induced by the biodegradable polymer scaffold itself. The engineered polymers were clearly associated with faster epithelization, richer neovascularization, and higher levels of organization of the "neoskin" than were the acellular ones. Although no normal skin adnexa were observed in the engineered areas up to 2 months after implantation, the progression of their histological appearance allows us to speculate the possibility of emergence of such adnexa at a later time. The long-term evolution of this fetal neoskin remains to be determined.

Fig 5. Normal skin histology of an 8-week-old lamb. (H&E, original magnification ×25.)

Videofetoscopic surgery is a promising minimally invasive technique still in its infancy.[19-24] Although preterm labor remains a limiting factor, fetal tissue harvesting is certainly feasible with instrumentation currently available. We considered the use of semiflexible balloon-tipped cannulas beneficial as a means to prevent dissection of the gestational membranes. Because these cannulas were not available in 2 mm diameter, we operated through 5-mm ports and used 2-mm instruments. The 10-mm port was used solely for the application of titanium clips, which were used for hemostasis of the harvested area. With the fast improvements and increased availability of smaller minimally invasive instruments currently in progress, it is likely that exclusively 2-mm ports, or smaller, could be used for these procedures in the near future.

Although warmed saline amnioinfusion is accepted as the more physiological medium for videofetoscopy, it is related to optic limitations. We were able to overcome such optic limitations in some animals by the use of medical air, without any evident harmful effect to the fetus, as evidenced by the high fetal survival rate. Carbon dioxide was not considered an option because of its previously described induction of fetal acidosis.[25]

It has been shown that fetal skin biopsy can be performed under ultrasound scan guidance.[26,27] In light of the high expansion rate that we observed with the dermal fibroblats, it is reasonable to consider ultrasound-guided fetal skin sampling as, perhaps, a viable way to obtain skin specimens for engineering purposes. A possible drawback is the smaller specimen size when compared with the ones obtained through videofetoscopy. This remains to be assessed.

The concept of skin replacement through the method hereby presented may prove useful for the treatment of certain human congenital anomalies such as giant neoplasias, ectopia cordis, and other body wall defects in which there may not be enough skin for coverage of the defect during surgical reconstruction in the neonatal period. Also, one could envision the concept of videofetoscopically assisted fetal tissue engineering as a means of definitive perinatal surgical treatment applicable to a number of other congenital deformities amenable to be diagnosed prenatally. Efforts in that direction are currently ongoing at our institution.

ACKNOWLEDGMENTS

The authors are indebted to Michael Chin, Niels Lausen, Laurie McCarthy, and Cynthia Barlow for their excellence in laboratory assistance.

REFERENCES

1. Rheinwald JG, Green H: Epidermal growth factor and the multiplication of cultured human epidermal keratinocytes. Nature 265:421-424, 1977

2. Watt FM, Green H: Stratification and terminal differentiation of cultured epidermal cells. Nature 295:434-436, 1982

3. Gallico GG, O'Connor NE, Compton CC, et al: Permanent coverage of large burn wound with autologous cultured human epithelium. N Engl J Med 311:448-451, 1984

4. Bell E, Ivarsson B, Merrill C: Production of a tissue-like structure by contraction of collagen lattices by human fibroblasts of different proliferative potential in vitro. Proc Natl Acad Sci U S A 76:1274-1278, 1979

5. Green H, Kehinde O, Thomas J: Growth of cultured human epidermal cells into multiple epithelia suitable for grafting. Proc Natl Acad Sci U S A 76:5665-5668, 1979

6. Rennekampff HO, Hansbrough JF, Kiessig V, et al: Wound closure with human keratinocytes cultured on a polyurethane dressing overlaid on a cultured human dermal replacement. Surgery 120:16-22, 1996

7. Yannas IV, Burke JF, Orgill DP, et al: Wound tissue can utilize a polymeric template to synthetize a functional extension of skin. Science 215:174-176, 1982

8. Heimbach D, Luterman A, Burke J, et al: Artificial dermis for major burns. A multi-center randomized clinical trial. Ann Surg 208:313-320, 1988

9. Stern R, McPherson M, Longaker MT: Histologic study of artificial skin used in the treatment of full-thickness thermal injury. J Burn Care Rehabil 11:7-13, 1990

10. Michaeli D, McPherson M: Immunologic study of artificial skin used in the treatment of thermal injuries. J Burn Care Rehabil 11:21-26, 1990

11. Murphy GF, Orgill DP, Yvannas IV: Partial dermal regeneration is induced by biodegradable collagen-glycosaminoglycan grafts. Lab Invest 62:305-313, 1990

12. Compton CC, Gill JM, Bradford DA, et al: Skin regenerated from cultured epithelial autografts on full-thickness burn wounds from 6 days to 5 years after grafting. A light, electron microscopic and immunohistochemical study. Lab Invest 60:600-612, 1989

13. Nave M: Wound bed preparation: Approaches to replacement of dermis. J Burn care Rehabil 13:147-153, 1992

14. Rouabhia M, Germain L, Bergeron J, et al: Allogeneic-syngeneic cultured epithelia. A successful therapeutic option for skin regenaration. Transplantion 59:1229-1235, 1995

15. Suzuki T, Ui K, Shioy N, et al: Mixed cultures comprising syngeneic and allogeneic mouse keratinocytes as a graftable skin substitute. Transplantion 59:1236-1241, 1995

16. Gilchrest BA, Karassik RI, Wilkins LM, et al: Autocrine and paracrine growth stimulation of cells derived from human skin. J Cell Physiol 117:235-240, 1983

17. Stanulis-Praeger BM, Gilchrest BA: Growth factor responsiveness declines during adulthood for human-derived skin cells. Mech Aging Dev 35:185-198, 1986

18. Phillips TJ: Cultured epidermal allografts—a temporary or permanent solution? Transplantation 51:937-941, 1991

19. Estes JM, MacGillivray TE, Hedrick MH, et al: Fetoscopic surgery for the treatment of congenital anomalies. J Pediatr Surg 27:950-954, 1992

20. Luks FI, Deprest JA, Vandenberghe K, et al: A model for fetal surgery through intrauterine endoscopy. J Pediatr Surg 29:1007-1009, 1994

21. Quintero R, Reich HJ, Prider KS, et al: Umbilical cord ligation of an acardiac twin by fetoscopy at 19 weeks gestation. N Engl J Med 330:469-470, 1994

22. Bargy F, Sapin E, Lewin F, et al: La chirurgie foetale. Rev Pratic 44:1719-1723, 1994

23. van der Wildt B, Luks FI, Steegers EA, et al: Absence of electrical uterine activity after endoscopic access for fetal surgery in the rhesus monkey. Eur J Obstet Gynecol Reprod Biol 58:213-314, 1995 (letter)

24. Quintero RA, Hume R, Smith C, et al: Percutaneous fetal cystoscopy and endoscopic fulguration of posterior urethral valves. Am J Obstet Gynecol 172:206-209, 1995

25. Luks FI, Deprest J, Marcus M, et al: Carbon dioxide pneumoamnios causes acidosis in fetal lamb. Fet Diagn Ther 9:105-109, 1994

26. Elias S, Simpson JL, Holbrook K: Fetal skin, liver, and muscle sampling, in Simpson JL and Elias S (eds): Essentials of prenatal diagnosis. New York, NY, Churchill Livingstone, 1993, pp 77-89

27. Elias S, Emerson DS, Simpson JL, et al: Ultrasound-guided fetal skin sampling for prenatal diagnosis of genodermatoses. Obstet Gynecol 83:337-341, 1994